JUN -4 1948

Vol. 23 APRIL, 1948 No. 4

SURGERY

A Monthly Journal Devoted to the Art and Science of Surgery

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APR 1 1948

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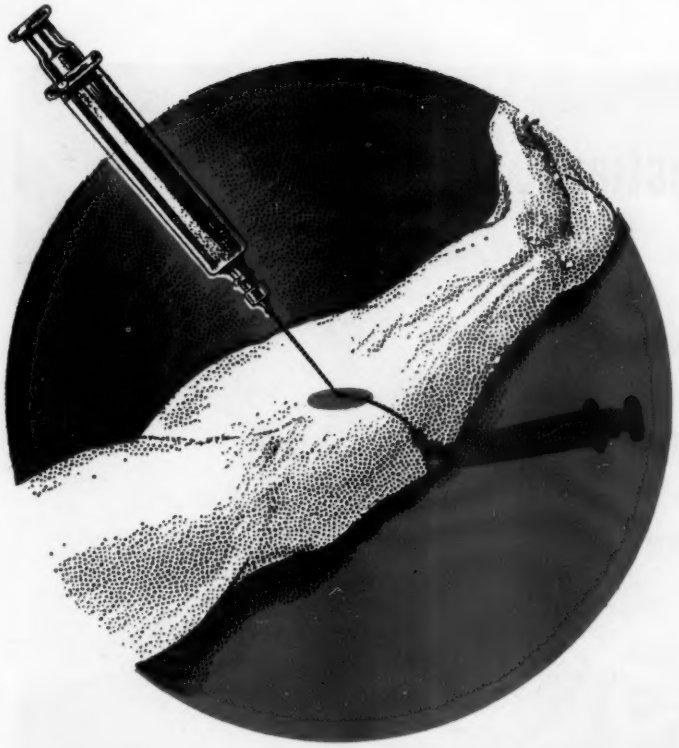
Vol. 23, No. 4, April, 1948. Surgery is published monthly by The C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, Mo. Subscription price: United States, its possessions, Pan-American Countries, $10.00 a year; Canada and Foreign, $11.00. Entered as Second-Class Matter January 20, 1937, at the Post Office at St. Louis, Missouri, under the Act of March 3, 1879. Printed in U. S. A.



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1. Arbesman, C.E., et al., Jl. of Allergy 17:275, Sept. 1946
2. Feinberg, S.M., and Friedlaender, S., Am. Jl. Med. Sci. 213:58, Jan. 1947.
3. Fuchs, A.M., et al., Jl. of Allergy 18:385, Nov. 1947.

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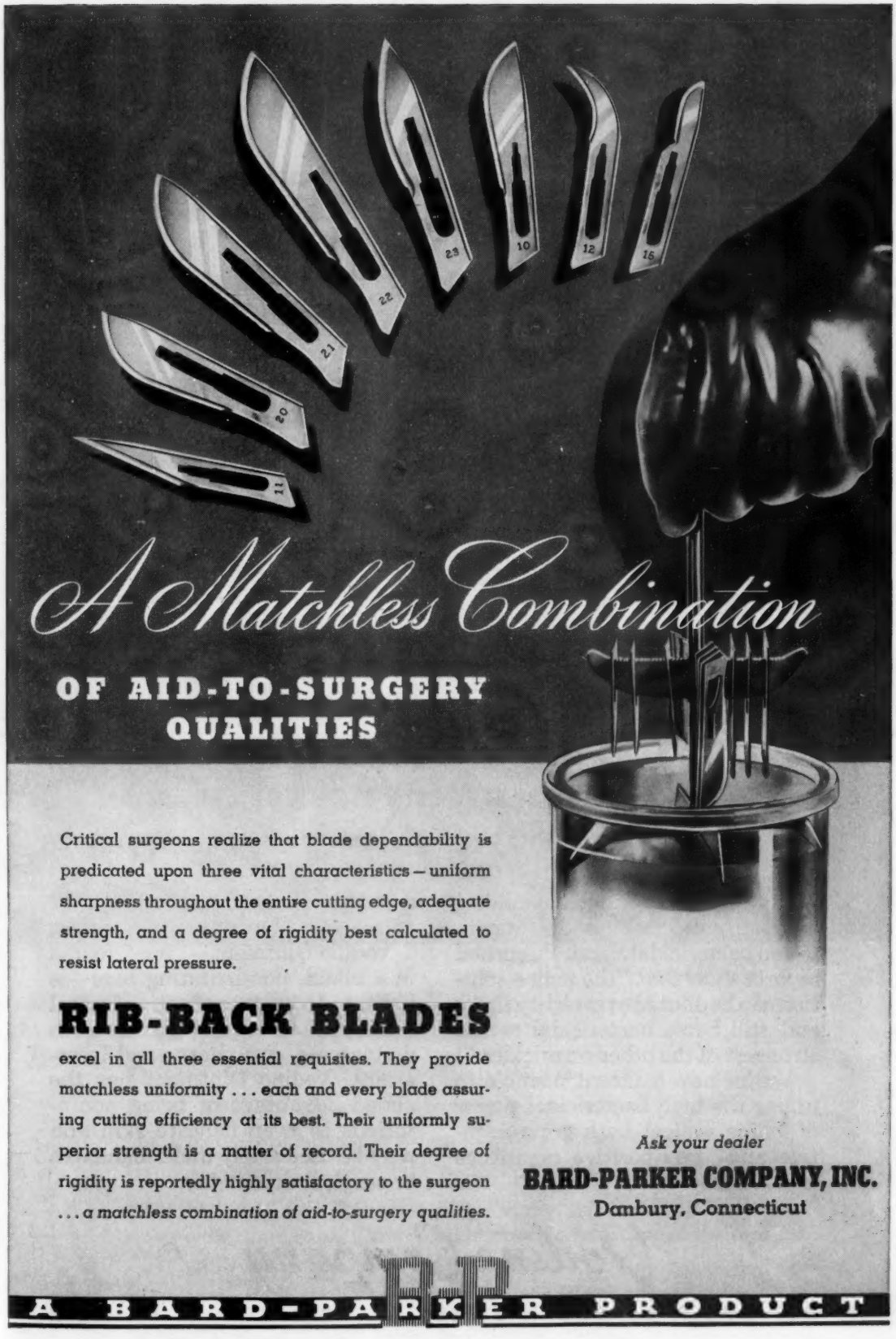
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1. New England J. Med. 213:279

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SUTUREGRAM

NUMBER SIX IN A SERIES

Knots

The set of first knot determines whether the suture will compress the tissues.

First knot set tightly
produces small circle.
Tissues compressed and
anemic. Blood vessels occluded

First knot set properly
produces larger circle
Tissue not compressed
Good blood supply
even when edema
develops 48 hrs. later

First knot set too tightly for
following reasons:
(1) Attempt made to
approximate widely
separated tissues

(2) Large suture
employed. Fine sutures break under
excessive tension (3) In order to prevent
slipping of first knot while tying second

SUTUREGRAM

NUMBER SIX (CONTINUED)

Slipping of first knot is prevented by

(a) extra loop in first knot (surgeons knot)

(b) pulling one end quickly toward other (for skin sutures)

(c) Maintenence of slight tension on first knot

Security of second knot maintained by

(1) tying third knot

(2) leaving long ends (too much foreign body)

(3) tying all knots flat

no grannys

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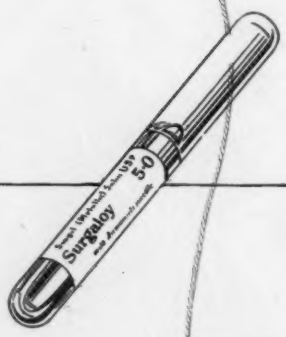

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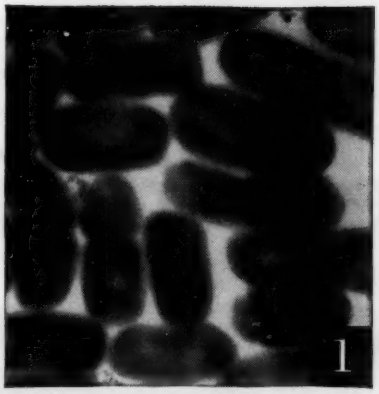

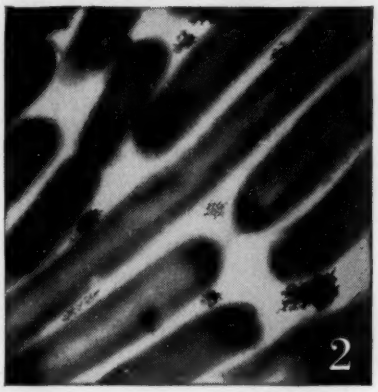

Micrographs approx. 10,500 X

Double action against K. pneumoniae...with SQUIBB streptomycin

bacteriostatic action of Squibb Streptomycin against *K. pneumoniae* is indicated in the accompanying direct transmission electron micrographs.

1. Normal Friedlander's bacillus. Note normally dividing cells in center of picture.

2. Organisms, after 18 hours exposure to Squibb Streptomycin in a concentration of 0.05 mmg. per ml. Cell growth continues, but normal division has been inhibited. Note enormously elongated cell which extends across four or five microscopic fields. Such cells reach a maximum length and die of old age. Note loss of surface definition in other cells.

bactericidal action of Squibb Streptomycin against *K. pneumoniae*, occurring simultaneously with the bacteriostatic action, is indicated in these electron microscope pictures of shadowcast specimens.

3. Normal Friedlander's bacillus coated with gold to give relief by the shadowcast technique.

4. Friedlander's bacillus after 18 hours exposure to Squibb Streptomycin in a concentration of 0.05 mmg. per ml. Cell wall shows advanced disintegration. Cytoplasm appears to have erupted through hole in cell wall and to have spread over partially collapsed cell, which is probably dead.

This double antibacterial action – bacteriostatic and bactericidal – against *K. pneumoniae* was secured with Squibb Streptomycin, a preparation of uniform potency and highest purity. Given in adequate dosage against susceptible organisms Squibb Streptomycin assures maximum therapeutic effect.

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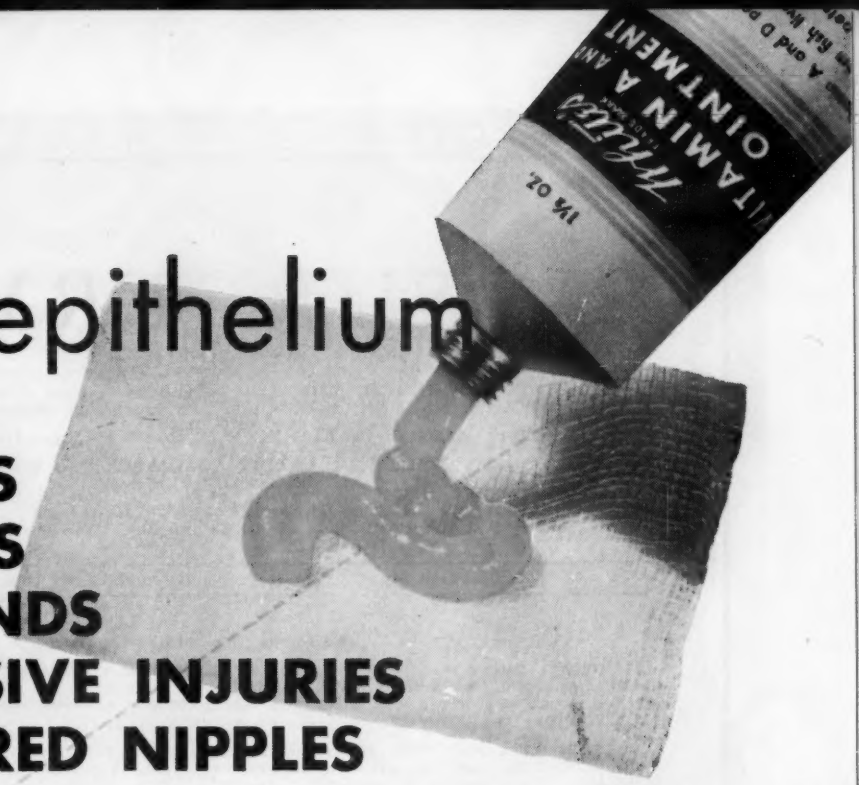

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Great Britain Agents: Henry Kimpton, Ltd., 26 Bloomsbury Way, London, W.C.1.
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Published Monthly. Subscriptions may begin at any time.

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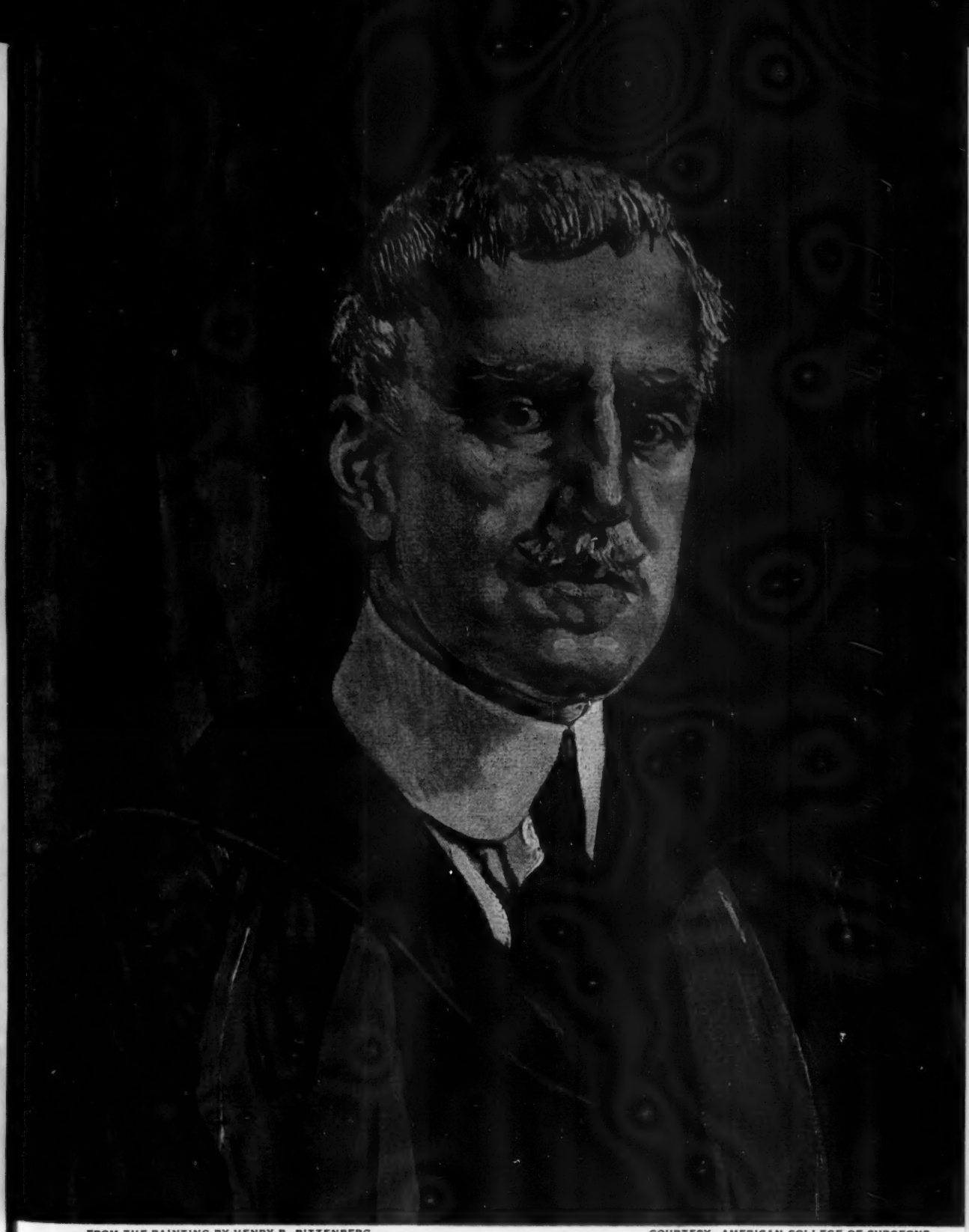

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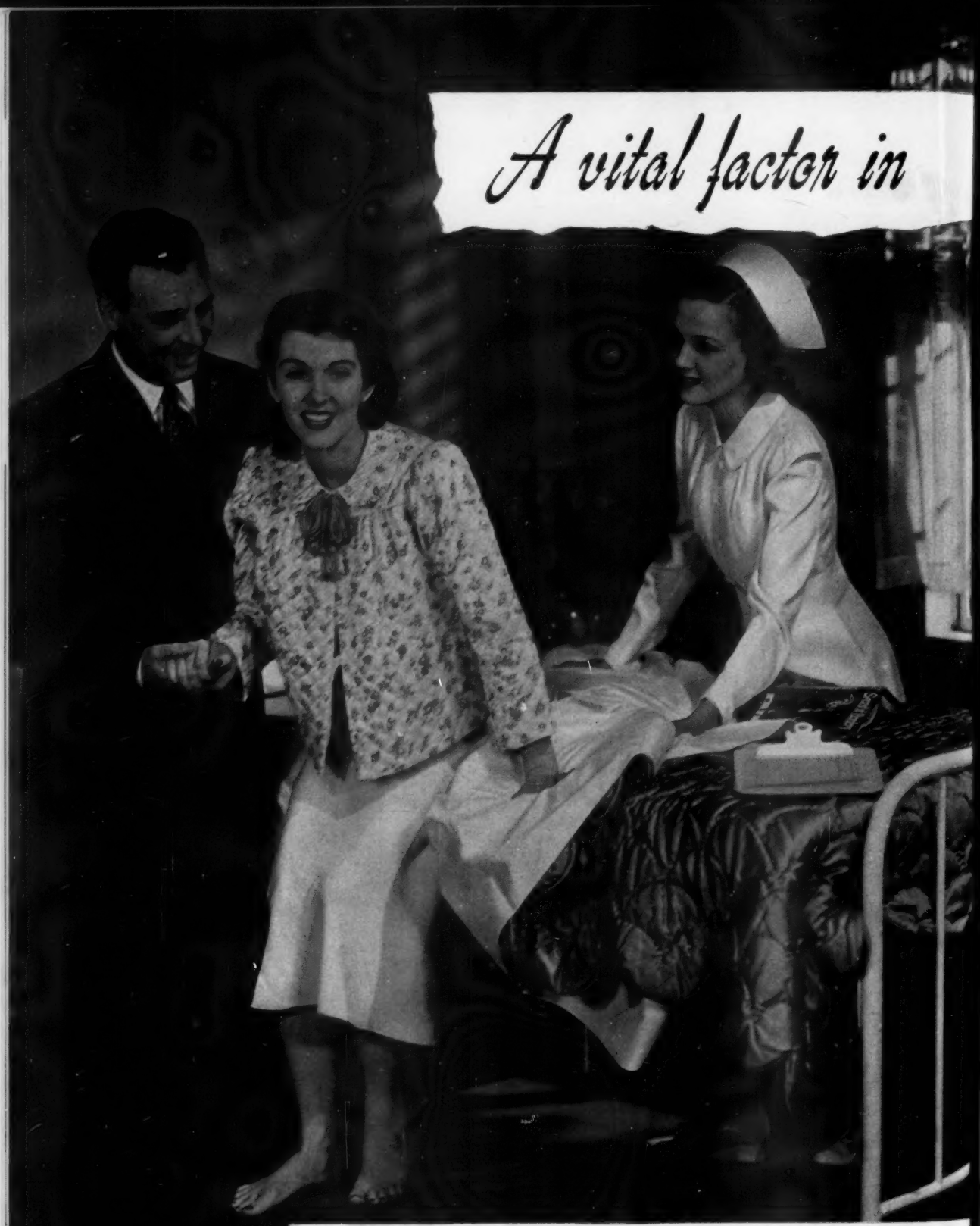

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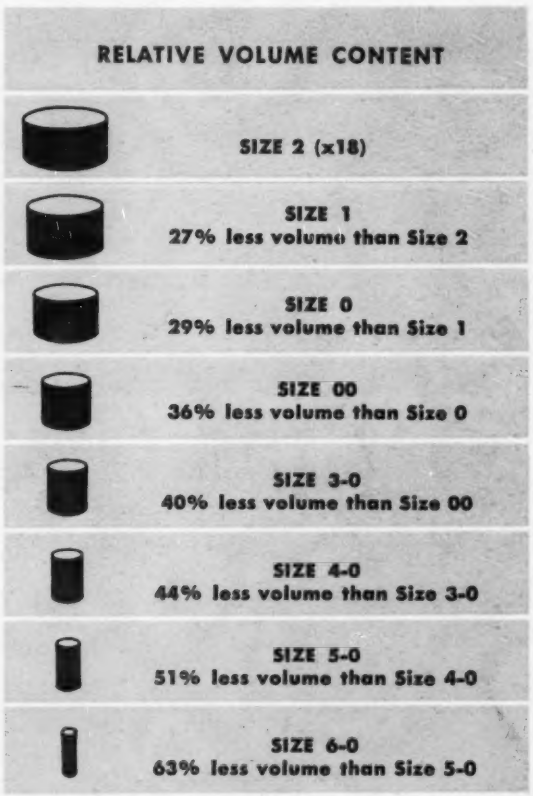

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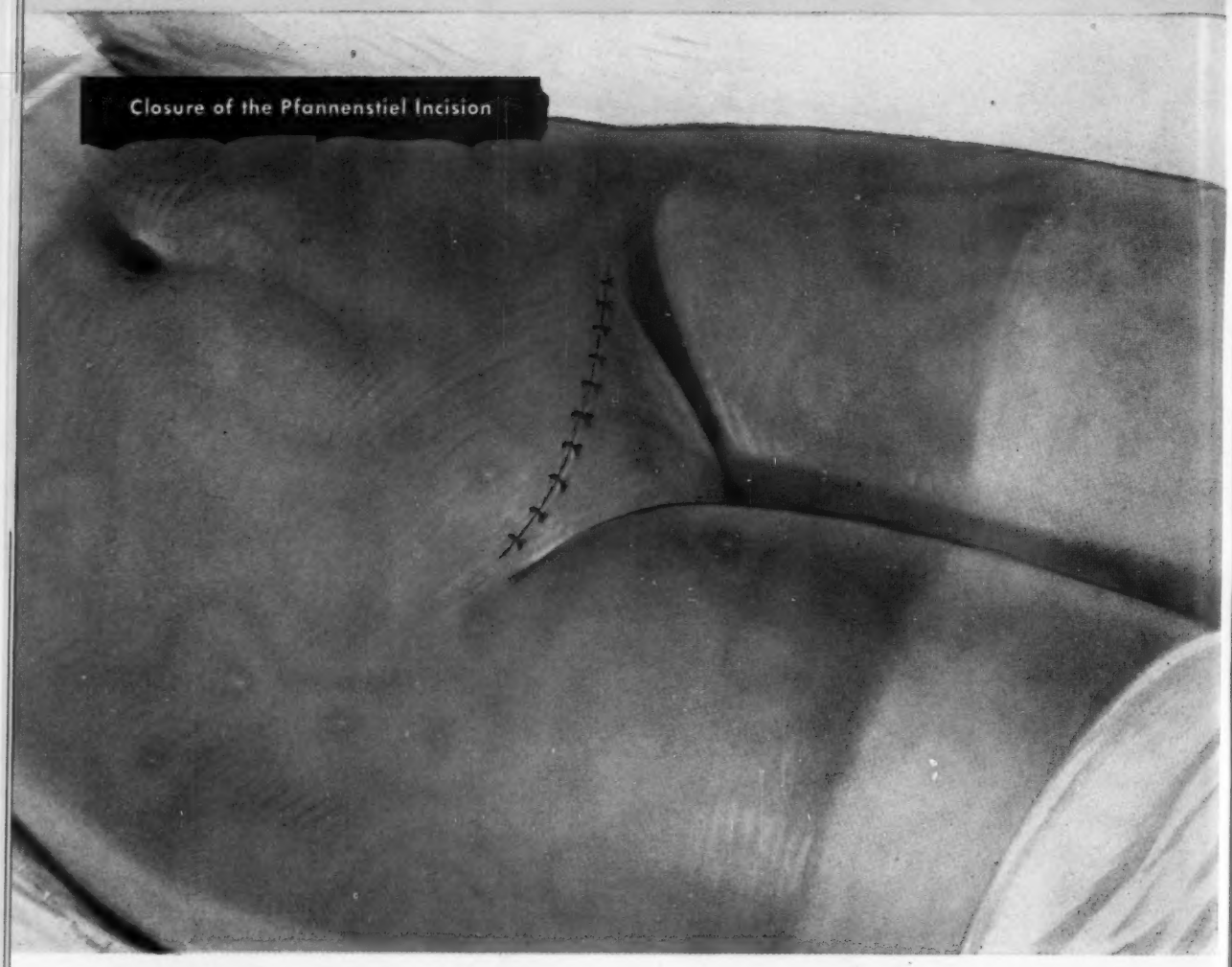

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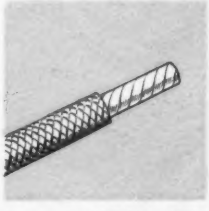

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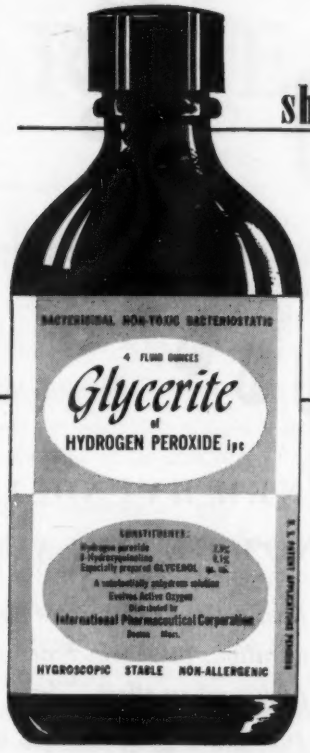

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SURGERY

VOL. 23 APRIL, 1948 NO. 4

Original Communications

THE CHANGING STATUS OF SURGICAL CARE

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I HAVE the most pleasant memories of my first visit to Rochester when as a very young surgeon I was told by the late John B. Deaver to take a vacation by visiting certain surgical clinics. Shortly after my arrival at the Clinic I met Dr. Judd, and I followed him closely for a week.

I saw him as a skillful surgeon. I saw him as a teacher interested in young men, offering sound advice from a life full of rare experiences. I remember well his taking me to a Wednesday evening staff meeting where I was shown a tragic accident which occurred during a supravaginal hysterectomy, and I well remember his admonition to me later, "Such tragedies happen to all surgeons—rarely to the prepared surgeon, but all too frequently to those who are not so well prepared." His terminal illness occurred, I believe, while he was on his way to Philadelphia to lecture.

With the acceptance of the antiseptic and later the aseptic discipline in surgery, "areas which previously had been denied the most intrepid of surgical adventurers were opened to all surgeons." Thus in the latter part of the nineteenth century and the early part of the present century emphasis was placed chiefly upon the technical aspects of surgery. The surgery of the body cavities took on a new birth, but the morbidity and mortality of many operative procedures, both old and new, were still high. This was in part due to the lack of knowledge by many surgeons of the normal physiology of the areas being subjected to operation and to an even greater ignorance of the deviations from the normal which occurs during disease. The responsibility for these circumstances was not solely the surgeon's. The frontiers of operative effort were extending so rapidly that physiologic and biochemical knowledge could not keep pace with them.

The Judd Lecture, given at the University of Minnesota, April, 1947.
Received for publication, Aug. 12, 1947.

I am reminded of an incident that occurred at a meeting of the British Physiological Society at Edinburgh in 1927. A symposium on the spleen was being held under the chairmanship of Sir Edward Sharpey-Shaefer. I sat next to Lord Moynihan for two hours while he became more and more restless. Finally after Professor Tait had discussed certain aspects of the spleen of fish Moynihan arose and said, "I have listened patiently for several hours but I have heard nothing that will help me in the care of patients with splenic disease." Sir Edward answered, "You must have further patience. Eventually we will be able to help you; perhaps what has been related this morning will be of help when it is better understood."

The high mortality which followed operations for thoracic empyema in the army camps during the influenza epidemic of World War I provides an excellent example of the failure of surgeons to use existing physiologic knowledge. In a few camps young surgeons, possibly as the result of superior physiologic training and possibly because of a lack of surgical skill, used interrib puncture instead of the traditional operation of rib resection. They placed the tube draining the thorax under water in some instances and in others applied suction to it. The methods which they used prevented pneumothorax and mediastinal shift. In these camps the mortality was relatively low; in others it was shockingly high.

It remained for Evarts Graham and his co-workers on the Empyema Commission to correlate physiologic, bacteriologic and pathologic knowledge to the immediate problem and a new era in thoracic surgery was opened. DuBois made the first careful studies on the nutrition of these patients and demonstrated how important it was that adequate nutrition be maintained during the period of recovery and convalescence.

George Crile had for some years been interested in certain phases of shock, in anesthesia, and in some of the problems of hyperthyroidism. He had tried to make surgeons realize that it was their responsibility to become more deeply interested in the problems with which they daily came in contact. It is true that his observations were not always correct nor his deductions always sound, but he stimulated an untold amount of research by clinicians and scientists which has been of immense value. Crile more than any other American surgeon of his time talked of improving pre- and postoperative care.

The "elder statesmen" at Rochester, of whom Dr. Judd was one, early realized the effect which scientific effort would have on the practice of medicine and surgery. Kendall, Mann, Rosenow, and many others were brought to the Clinic, not to engage in clinical medicine or surgery, but to expand the existing knowledge of the pathologic physiology of disease. Judd became a master surgeon because of his ability to utilize such contributions, as they became available, in the therapy of many surgical disorders. One only need read the contributions to surgical literature of which he was a joint author to be assured that he provided the incentive for many young men to study further the problems which they were daily meeting at the operating table and at the bedside.

It was during the period of the early twenties that one could recognize a more concerted effort by surgeons to reduce the morbidity and mortality of

contemporary surgical operations by the introduction of improved methods of preoperative preparation and postoperative care. As the physiologist and the biochemist developed new techniques for investigation, they made a new body of information available. The surgeons, who could understand such knowledge, began here and there to apply it to the problems daily being met in the surgical clinic.

Such a change has had a profound influence on surgery. The borders of surgical effort were more widely extended. Many diseases which were not amenable to cure by medical therapy became subjected to surgical therapy and while cure has not always been attained a great measure of relief from suffering has been afforded. The morbidity and mortality of many of the newer, and most of the older, operations were greatly reduced. The surgeon began to be less afraid of becoming too scientific, and the pure scientist came to realize that the fundamental observations from the laboratory were more apt to find successful clinical application through the efforts of thoroughly trained young clinicians. A mutual respect and understanding arose between them.

As one reviews these early efforts in improving care and in extending the technical aspects of surgery, one might well gain the impression that surgeons are inclined to be faddists rather than critical scientists. We have gone through various eras in care and in technique. Intravenous therapy was slow in being adopted, but once it was we nearly forgot that the gastrointestinal tract was designed for a specific function and should be used whenever possible. Many surgeons did, and some still do, repair all inguinal hernias in the same way, or do every cholecystectomy or gastrectomy or thyroidectomy alike. Surgeons too frequently have become so concerned with methods that they have forgotten the importance of principles and the variable reaction of patients to disease. Too great emphasis has often been placed upon limited aspects of disease and upon certain specific aspects of care instead of realizing the interrelationships of many biologic processes.

In spite of these excesses I believe that a healthy process of development has taken place and that each phase of this development has added greatly to the knowledge of disease and to the safety of anesthesia and operation. Empiricism in pre- and postoperative care and in operative technique has become less evident although it has not disappeared, while sound clinical investigation has come to play an ever-increasing role in therapy in its broadest sense.

The Development of Surgery.—Harvey Cushing's intimate knowledge of cerebrospinal and endocrine physiology led to the development of neurosurgery as a special field of surgical endeavor, and he will always be looked upon as the first genius of this specialty. He insisted on painstaking histories of patients. He did not tolerate the divorce of the hand from the mind. A surgeon was to him an internist and something more.

The neurosurgeon must be a neuroanatomist, neurophysiologist, neuropathologist, and neurologist. Cushing stimulated an untold amount of basic and applied research, and he was respected by clinicians and scientists the world over. He won for neurosurgery a place which it had never before attained, and

he and his disciples were responsible for a complete change in the surgical approach to many neurologic disorders.

Willy Meyer and Howard Lillienthal were among those who early espoused the cause of a surgical attack on certain intrathoracic diseases. The development of the negative pressure chamber was an attempt to meet the physiologic disturbances associated with intrathoracic exploration. It remained for Evarts Graham, John Alexander, Edward Churchill, and others to make the surgery of intrathoracic and intrapulmonary suppuration and benign and malignant tumors as safe as much of the intra-abdominal surgery. The surgery of pulmonary tuberculosis has provided new hope to sufferers from what previously was considered a purely medical disorder. And yet it may well be that streptomycin or some other chemotherapeutic or antibiotic agent may again return this disease to the category of nonsurgical diseases.

The brilliant work of Alfred Blalock who with Helen Taussig has provided a solution for the tetralogy of Fallot, of Robert Gross and Clarence Crafoord in the therapy of aortic coarctation, and of Reginald Smithwick in the surgical therapy of essential hypertension provides further evidence of the changing status of surgical care. The symptoms of many peripheral vascular lesions can now be relieved by sympathectomy. Embolectomy is today so common that a successful operation causes little comment. Already some men are devoting their entire effort to the problems presented by vascular disease.

D. W. Gordon Murray, at a recent meeting of the American Surgical Association, reported that when an area of experimentally induced cardiac infarction was excised before relaxation, dilatation, and paradoxical pulsation of the heart had taken place, cardiac failure and ventricular fibrillation did not occur, while death occurred in all control animals. We shall not convince our cardiologic confreres that this procedure deserves immediate clinical application, but Murray's concept bears testimony to the constantly widening interest by surgeons in what for years have been considered medical problems. And who would be so bold as to deny that before another decade has passed the outlook of coronary disease which claims so high a toll of our profession may in part be amenable to surgery.

For nearly two decades there has been general agreement that the best therapy for a gastric or duodenal ulcer, once a medical program failed to give relief, is a radical resection of the stomach and the ulcer-bearing portion of the duodenum if the ulcer is in that part of the bowel. It is, in my opinion, still the best operation for a gastric ulcer. The rediscovery by Dragstedt of the effect of vagus resection on total gastric secretion and hydrochloric acid production is another example of a physiologic approach to one of the most important characteristics of the peptic ulcer. An abundance of free acid induces chronicity of the ulcer, and is an important factor in the pain associated with the disorder. The etiology of these lesions is not yet clear although, as a result of the work done by Wangensteen and his associates, we know a great deal more than we did two decades ago. All are agreed, however, that an abundance of free hydrochloric acid plays an important part in the life history of these lesions.

Vagal neurectomy will not supplant radical gastric resection even for duodenal ulcer, but it provides a rational approach for the correction of one aspect of the pathologic physiology of this widespread disorder.

Many years ago Pasteur remarked, "Fate favors the prepared mind."

Those who have broadened and are broadening the horizon of surgical effort have had the necessary spirit of investigation in their fields of special interest. While in the main the fundamental work has been done by men in the basic sciences, a worth-while portion of it has come from the laboratories of surgical research.

The direction of surgical therapy must be more and more toward less destructive operations if lesser procedures can be found which will correct the pathologic physiology of a given disease. But until such methods are found, we must in certain instances move in an even more radical direction. Bold surgeons are now doing large operations for small tumors, and the end results of operation for many malignant tumors are showing definite improvement.

It is not possible to review all of the changes that have taken place and are taking place in operative effort, for they cover nearly the entire field of surgery. This is the result of many forces, some of which I have already referred to. It is the result of the greater responsibilities afforded young men of vision, who with modern training and an appreciation of the relationships between research and practice, have not been tied down by the dogma and empiricism of the so-called golden age of surgery. It is the result of improvements in anesthesia and anesthetization and in pre- and postoperative care.

Anesthesia.—Anesthesia, as we know it today, has contributed much to the maintenance of physiologic balance in patients during operation and in the postoperative period. Adequate working conditions for the surgeon are provided without the severe depression of body function which formerly was so common. Tissue damage secondary to anoxia is minimized by support of the circulation and inhalation of adequate concentrations of oxygen. The acidosis of deep ether anesthesia is recognized and avoided. Relaxation of the abdominal wall is secured, not by prolonged narcotic poisoning, but with spinal anesthesia or general anesthesia supplemented with a curare-like substance. The physician anesthetist no longer strives for a reduction in anesthetic mortality—this he has largely achieved. The goal now is a reduction in morbidity, a lowered incidence of postoperative nausea and vomiting, of atelectasis and pneumonia, of malaise and psychic depression. The anesthetist is moving in the direction of techniques which will accomplish these purposes to an even greater extent.

Preoperative Preparation and Postoperative Care.—The surgeon now recognizes that expert preoperative preparation and postoperative care are essential parts of surgical therapeutics. The operation remains, and probably always will remain, the most dramatic part of the surgeon's work, but a successful operation now means a well patient. The surgeon, as contrasted with the operator, is better equipped critically to evaluate the newer adjuncts to surgical therapy to the end that patients previously denied operation will receive it and that the morbidity and mortality of many operations will constantly decrease and the end results constantly improve. I can do no more than briefly review some of

these concepts which have had and are having a profound influence in altering the status of surgical care.

Gastrointestinal Intubation.—The report of Wangensteen and Paine in 1933[1] on the use of gastric suction drainage marked a milestone in the care of patients requiring major abdominal surgery, in the therapy of acute intestinal obstruction, and in the control of fluid and electrolyte balance. Suction drainage is now utilized in every clinic to keep the stomach empty before operation, transforming what previously was a cesspool into an empty and clean viscus. Radical gastric resections can be done and the remaining gastric segment kept empty in the period immediately following operation. This practice has led to a substantial reduction in the morbidity and mortality of gastric operations. Acute gastric dilatation has now become a rarity in our clinics.

The development of the Miller-Abbott tube and its use by Johnston and Abbott[2] in acute intestinal obstruction unassociated with gangrene was a further step in gastrointestinal intubation. Wangensteen and Paine[1] had previously reported the use of short tube intubation in acute obstruction. There can be no doubt that in their hands and in others the use of suction drainage resulted in a substantial reduction in the mortality of this condition. In the best of clinics the mortality of acute intestinal obstruction prior to intubation was approximately 40 per cent. With the use of short tube intubation Wangensteen[3] reported a mortality of 17.1 per cent. Abbott and Johnston[4] reported a mortality of 9.3 per cent with the use of the Miller-Abbott tube, while with the same tube Whipple[5] and Leigh, Nelson, and Swenson[6] reported a mortality of 2.8 and 5.9 per cent, respectively.

Intubation has made it possible to maintain more accurately the fluid and electrolyte balance. With its use the pathologic effects of intestinal distention can be overcome, thus improving the general and local circulation and reducing the effects of distention upon respiration. It has made possible single stage resections of the right half of the colon, thus reducing the hazards of two or more operations. It has permitted the surgeon to take the poor-risk patient, dehydrated, distended, and in peripheral vascular collapse, and rehabilitate him to the extent that operation can be done with safety. It has proved to be one of the great aids to the abdominal surgeon.

It has stimulated an unbelievable amount of research and still more remains to be done. For many years we have spoken of paralytic ileus in association with diffuse peritoneal infection and yet in the presence of this condition I have seen the Miller-Abbott tube pass freely through the small bowel. Surely this could not take place if the bowel were paralyzed in the traditional sense.

Peripheral Vascular Collapse.—In 1918 Frank Mann[7] wrote of shock as follows: "A review of the results obtained in the extensive amount of work that has been done on the problem of shock, both experimentally and clinically, makes the point I have repeatedly emphasized particularly clear, namely, that the condition the surgeon calls shock may be due to a variety of causes. The variation in the primary etiologic factor in a condition in which identical clinical symptoms occur is probably the cause of the more or less contradictory conclusions arrived at by investigators, both experimentally and clinically."

In the intervening years a great deal of work has been done in this important field, and the advent of World War II stimulated further intensive research. It is now time that we attempt to reorient ourselves in regard to this condition. Recent carefully controlled investigations have cast doubt upon the concept that there is a generalized increase in capillary permeability in regions remote from trauma or even following severe hemorrhage.

Cournand and his associates[8] have shown that the essential finding in clinical shock in man is an inadequate venous return of blood to the heart with diminished cardiac output. A reduction in the circulating blood volume is, in most instances, responsible for these changes. In severe states of peripheral vascular collapse in man the blood volume may be reduced as much as 40 per cent or more. It is a curious circumstance that in the collapse of the circulation associated with some abdominal injuries and in severe infections the reduction in the effective blood volume may be much less than this.

Investigators and clinicians have long been baffled by the fact that with effective therapy some patients achieve homeostasis fairly promptly while others fail to do so. The work of Frank, Seligman, and Fine[9] has shed new light on this circumstance. They have concluded that "advanced shock constitutes a state of progressive deterioration which is not amenable to the types of therapy now available, probably because fundamental biochemical changes have developed as a result of a prolonged deficiency of capillary blood flow. These changes may result from changes predominately involving one vital organ, such as the liver, or from widespread cellular damage." Recently these authors have obtained further evidence which implicates the liver as the conditioning organ in the development of irreversible shock.[10]

The late stage of peripheral vascular collapse, so-called irreversible shock, cannot be overcome by restoration of, or even an increase over, the original blood volume. But surgeons now know that the irreversible stage of shock can be prevented by early and vigorous therapy directed toward maintenance of an adequate blood volume.

In the search for blood substitutes Wangensteen and his associates turned to bovine plasma. While the use of this material did not prove practical, it was helpful as a pilot experiment. Edwin Cohn fractionated human plasma and isolated a group of substances of great value to clinical medicine and surgery.

Two general statements can be made on the basis of the military experience with infusion fluids. First, while plasma or albumin solutions may be used as a stopgap in hemorrhagic shock, patients need whole blood to put them in shape for surgical procedures and to speed convalescence. Second, while concentrated serum albumin is effective in well-hydrated patients, it is relatively ineffective in dehydrated persons, such as desert troops. The military experience further emphasized the necessity of adequate volume therapy in shock. If a patient has lost 40 per cent of the effective blood volume, too much should not be expected from therapy which provides but 10 per cent of that lost. Lives can be and are being saved every day by adequate replacement therapy. For effective replacement one must determine the blood volume, and this is now being done daily in many of our hospitals.

To reduce the disastrous effects of irreversible shock we must rapidly and continuously replace a depleted circulatory volume, and we must just as effectively prevent overwhelming sepsis. In replacement therapy either plasma, gelatin, albumin, or whole blood should be used, and these will be found to be effective if the hypotension has been of short duration. Once significant metabolic changes have occurred in important viscera as the result of prolonged hypotension there is no therapy which today offers any hope of reversing the end stages of peripheral vascular collapse.

Chemotherapy.—In few fields of therapeutics has such progress been made as in the control of bacterial infections. For some years some progress had been made in our knowledge of infections and their control, but the contributions to the chemotherapy of bacterial infections during the past decade have had a profound influence on surgical care. The ability of the sulfonamides, penicillin, and streptomycin to check the spread of invasive infection is of enormous importance to surgeons. While our knowledge of the mechanism by which they act is still far from complete, thousands of patients throughout the world are deriving benefit from these substances which limit the ability of bacteria to survive in the tissues of the body.

Anderson,[11] working in our laboratories in 1934, after studies on the control of infections in wounds concluded that the major factor in the failure to control infection was the presence of necrotic tissue. He found that once the necrotic tissue was removed local surface infection was unimportant in the healing of a wound, for the wounds then proceeded to heal according to the Carrel-du Nöuy[12] formula. The brilliant work of Churchill[13] in formulating the reparative program in surgery in the Mediterranean Theater of Operations, which was of such great value to our injured troops, provided clinical substantiation of Anderson's carefully conducted experiments.

In the many thousands of battle casualties coming under the direct and immediate care of the 20th General Hospital, not a single patient succumbed to invasive streptococcic infections. Some died from peritonitis, some from meningitis, and others from gas gangrene, but the experiences of World War I, where thousands died from a spreading hemolytic streptococcic infection, were not repeated in World War II. While chemotherapy does not supplant the sound surgical practice of débridement, it serves as an important adjunct to this method of therapeutics.

Erysipelas is now so rare that we seldom find a patient with this disease to show students. Mastoiditis and thoracic empyema are fast becoming as rare. The bacterial population of the intestinal tract can be materially reduced prior to bowel resection by the use of certain sulfonamides and to an even greater extent by streptomycin.

The unfavorable course of experimental and even human peritonitis can be favorably influenced by sulfonamide, penicillin, and streptomycin therapy in spite of the fact that many of the pathogenic organisms found in peritonitis are not readily susceptible to these substances. It may well be that with the substantial reduction in organisms resulting from specific therapy the defense

mechanisms within the abdomen, including the ability to mobilize large numbers of phagocytes, are sufficiently effective to overcome the residual infection. In the management of peritonitis the maintenance of the fluid and electrolyte balance, the relief of distention, and the use of chemotherapy all play an important part.

The dramatic control of these and many other serious infections by chemotherapy may well discourage investigators from attempting to solve fundamental problems related to infection. All serious acute infections and many chronic ones are associated with profound disturbances in normal physiologic function. We must know more about these.

Paul Cannon's[14] work on antibody production and phagocyte formation in protein deficiency is an example of such disturbance. The fact that many serious infections can now be prevented and others controlled must not deter investigation in this important field.

Thrombosis and Embolism.—Venous thrombosis and pulmonary embolism have long offered a tantalizing challenge to the medical profession. Kirby[15] in a recent article stated the following facts:

> Important recent concepts which are rapidly gaining acceptance are the following:
>
> 1. Venous thromboses of clinical importance, including those which cause pulmonary embolism, usually originate in the veins of the lower extremities, principally in veins below the knee.
>
> 2. Venous thrombosis and pulmonary embolism occur as commonly in the "medical" diseases as they do following surgical operations.
>
> 3. Venous thrombosis in the lower extremities of middle-aged and elderly persons confined to bed is a frequent occurrence, being found in about 50 per cent of such persons dying from all causes.
>
> 4. Acute thrombophlebitis and phlebothrombosis, or bland thrombus formation, are distinctly different pathological and clinical entities. In acute thrombophlebitis, which is readily recognized clinically by a marked inflammatory reaction and vasospasm, thrombi are usually firmly adherent to the walls of the involved veins. In phlebothrombosis, which often has minimal clinical symptoms and signs, or may not be recognized clinically, the thrombus is so loosely attached to the vein wall that it may be easily dislodged, with resulting pulmonary embolism.

At the Hospital of the University of Pennsylvania the incidence of fatal embolism has been about 1 in every 1,200 operations. Pulmonary embolism is responsible for about 5 per cent of all postoperative deaths.

In general, three measures are being used to reduce the incidence of fatal embolism. Early rising or ambulation has been advanced as a prophylactic measure against thrombosis and embolism. Van Jaseke,[16] Zava,[17] Leithauser,[18] and others have made remarkable claims for early ambulation as a means of reducing the incidence of phlebothrombosis and of fatal embolism. In our clinic the data are not nearly so striking. During the past eighteen months early rising has been practiced nearly routinely, and the incidence of phlebothrombosis has not been greatly affected.

John Homans[19] was the first to advocate ligation as a means of preventing fatal embolism. The usual site of ligation is the superficial femoral vein or the

profunda femoris. Numerous authors have advocated ligation of the inferior vena cava in the presence of thromboembolism. Allen[20] instituted the practice of prophylactic bilateral ligation before major abdominal operations, and he is convinced that this is a safe and lifesaving procedure.

It would be difficult to determine the number of prophylactic ligations that are now being done in surgical clinics in this country each month. It is even more difficult to justify the widespread use of the procedure on the basis of available statistical data. We have used it in several hundred patients as a prophylactic measure and following the development of phlebothrombosis of thromboembolism, and we are sure that some lives have been saved. It is, however, not entirely a harmless operation, for some of our patients have a residual edema which is troublesome, and others have developed skin changes which are at times most annoying if not alarming.

Heparin and dicumarol have been advocated for use as prophylaxis on the theory that it is increased coagulability of the blood that is responsible for venous thrombosis. Allen[20] has been a strong advocate of dicumarol therapy while Murray and Best[21] and Crafoord and Jorpes[22] have just as strongly supported heparin therapy.

It is an unfortunate circumstance that the advocates of one method of therapy are so positive that their method is the correct one. I am still unconvinced that in any one method we have the answer to this problem. If we were universally to reduce sedation before and after operation, if we were to bind the lower extremities from the time of admission of a patient until the time of discharge, perhaps we could reduce the incidence of phlebothrombosis and thus the incidence of thromboembolism.

Until significant data are available to prove the value of one method over another we are reducing sedation, binding the legs, and practicing early rising. When thrombosis appears, we have found it advisable to use heparin and dicumarol in certain cases and to ligate the veins in others. With such a program the incidence of fatal embolism has been materially below the previous fifteen-year average, but it must be stated that a longer experience will be necessary before data which are statistically significant are available.

Nutrition.—In few fields of pre- and postoperative care have such advances been made as in the field of nutrition. For years clinicians have believed that the nutritive state bore some vague relationship to resistance, but the complexity of this relationship is not yet solved. Varco[23] recently provided the best discussion I have seen of this important subject.

In the field of the vitamins alone great gaps in our knowledge are being filled. The administration of glucose by the intravenous routes demands an increased intake of thiamine, riboflavin, and niacin, and the administration of protein hydrolysates requires additional riboflavin because this substance is concerned with the utilization of certain amino acids.

Vitamin K has revolutionized the care of the jaundiced patient, and hemorrhage is no longer the major cause of death following operation. We have within a few short years nearly forgotten the anxiety which previously attended operations on the jaundiced patient.

Prolonged malnutrition leads to a reduction in the protein stores of the body and in the production of hypoproteinemia, the latter being a ready, although not always reliable, index of the extent to which the reserve stores of body protein have become depleted. The pattern is not always the same, as has been shown by the studies made by Keys and his associates[24] here at Minnesota.

When a protein deficiency exists with a severe anemia, the protein stores will be more rapidly replenished if the anemia is overcome by vigorous transfusions of blood, as suggested by George Whipple.[25] If this is not done ingested protein and minerals will be utilized first to overcome the anemia. The use of blood transfusions, in addition to adequate diet, when anemia and protein deficiency coexist, as they so frequently do, is thus placed on a sound clinical basis.

Injury, as well as disease, is frequently attended by prolonged periods of excessive nitrogen loss, and anesthesia and the very nature of the operation may impose a further drain upon an already depleted nutritional system. To what hazards are such patients exposed?

Cannon and his associates[26] have found that protein deficiency in the experimental animal is associated with a lowered activity of the antibody-producing mechanism and that the restoration of the depleted protein reserves results in the restoration of the normal capacity for antibody production. The data which they have collected strongly suggest that in the presence of a severe protein deficiency the "ability to acquire resistance quickly or to mobilize a specific immune mechanism effectively may also be impaired." In severe inanition the cellular tissues which supply phagocytes in large number undergo atrophy, and under such "circumstances the leukocytic tissues tend to revert to myeloblastic levels." Such tissues are not advantageously prepared to cope with acute infection by the liberation of adult phagocytes regardless of the amount of specific antibody which may be present. Protein depletion and malnutrition in this sense provide the circumstance where two of the most important biologic factors assisting in the control of infection are impaired.

As early as 1921 Whipple and Davis[27] showed that hypoproteinema conditioned the onset of shock following tissue injury. Ravdin, McNamee, Kamholz, and Rhoads[28] demonstrated that hypoproteinemia greatly increased the susceptibility to shock which resulted from hemorrhage.

Every surgeon of experience has observed how readily patients who are in a poor nutritional state develop peripheral circulatory collapse following anesthesia and operation. The reduced blood volume of these patients does not permit further great fluid loss before shock becomes evident.

The relationship of nutrition to wound healing is beyond question. In 1926 Wolbach and Howe[29] demonstrated that the specific important agent in the development of the intercellular cement substance was vitamin C. Later Lanman and Ingalls[30] showed that the tensile strength of healing wounds in guinea pigs was lowered in the presence of a C deficiency, and these findings were soon confirmed by Taffel and Harvey.[31]

In 1938 Thompson, Ravdin, and Frank[32] reported that in dogs suffering from a severe protein deficiency the healing of abdominal wounds was greatly delayed and wound infection and dehiscence were greatly increased. These observations made on experimental animals have since been confirmed by numerous investigators in man.

Donald Munro[33] first demonstrated the relationship of a protein deficiency to the failure of decubitus ulcers to heal, and his observations have been confirmed by Mulholland and his associates.[34] Every medical officer serving in general hospitals in this country during World War II became convinced that adequate nutrition was the most important factor in obtaining healing in such lesions.

Malnutrition, especially a severe protein deficiency, retards the laying down of callus in healing fractures. It plays a role in the healing of peptic ulcers. The exaggerated edema which occurs in the hypoproteinemic patient following operations on the gastrointestinal tract may so seriously retard normal function as to suggest a technical defect of the anastomosis. Malnutrition will accentuate many of the symptoms of hyperthyroidism, and the hyperthyroid patient who fails to gain weight in the preoperative period presents a more serious surgical hazard than does the patient who comes to operation with replenished body storehouses.

The value of a diet adequate in protein and carbohydrate, in vitamins and in total calories, in the preparation of patients with serious liver injury or fatty infiltration is now recognized by all surgeons.

The prolonged use of liquid and soft diets is an anachronism, and yet the traditional caution of our profession permits them to be used long after the period when a diet adequate in composition and in total calories would facilitate recovery and provide the building stones for more rapid and secure wound healing. Madden and his associates[35] have recently published important data from man in this regard. They found that of the two routes for supplying exogenous protein, the oral route was preferable. The intravenous route was valuable when oral intake was impossible or inadvisable. A pure amino acid mixture and a protein hydrolysate were not utilized as well parenterally as orally and neither was so well utilized orally as the natural food proteins.

These data are in agreement with those of Koop and associates,[36] who found that a positive nitrogen balance could be obtained in postoperative patients by the oral intake of 0.3 Gm. of nitrogen and 30 calories per kilogram of body weight per day, but that when intravenous therapy was utilized in such patients, the nitrogen intake had to be nearly doubled and the total calories increased by more than 30 per cent before a positive nitrogen balance was obtained. Intravenous therapy unless necessary is, therefore, extravagant and wasteful.

It is an unfortunate circumstance that the various nutrients have been considered all to frequently as independent entities. One group of workers is vitamin conscious, another protein conscious, and so on. It has been our experience, and I am sure it is the experience of others, that most patients suffering from a pronounced deficiency of nutrition have a complex deficiency.

We have passed through the carbohydrate era, the vitamin era, and are now in the protein era. Perhaps intensive interest in a special field has been helpful from the standpoint of clinical investigation, but the continuation of such limited interest retards rational therapy.

The best way to restore good nutrition is to feed the patient by mouth a diet adequate in carbohydrate, protein, and fat—a diet which contains the necessary vitamins and minerals. Only when the oral or orojejunal route is not available or when supplementation is necessary should parenteral therapy be employed.

Early Ambulation.—In 1899 Emil Ries of Chicago[37] advocated "some radical changes in aftertreatment of celiotomy cases," but the surgical profession as a group has continued to favor prolonged rest in bed as essential to recovery. During the past five or six years early ambulation has been receiving more widespread use. We had the opportunity to see it practiced in an extreme form in the Chinese Section of the 20th General Hospital. It was difficult to keep these patients in bed under any circumstances. They required less morphine than American patients, less catharties, less frequent catheterization after operation, and infinitely less nursing care, and yet the mortality in both sections of the hospital was nearly identical. The convalescence of the Chinese patients was so rapid that we were amazed.

It is a bit startling to many visitors to see our patients who have had major operations walking around within so few hours after operation. Only the very obese, those with severe cardiac conditions, and those with serious infection are permitted the traditional form of bed care. The physiologic and psychologic advantages of this program are numerous.

Early ambulation facilitates the earlier restoration of a positive nitrogen balance. It prevents the rapid deterioration of musculoskeletal tone. It improves the circulation. Nursing care is reduced because fewer enemas are necessary. Finally, the psychologic effects of early rising are incalculable. Once out of bed the patient becomes convinced that the surgeon "knows he is progressing normally toward recovery."

Prolonged bed rest encourages a vicious cycle; inactivity results in prolongation of the time necessary for the return of normal function, an extension of the period of intravenous therapy, and prolonged periods of a negative nitrogen balance. These we are sure of, but there is no need to discuss this subject further when so many of the fundamental studies on convalescence and rehabilitation were made by Keys and his associates at this school. The greatest fear of early rising has been that it may interfere with wound healing and thus increase the incidence of wound disruption. It has not done this in the Arabs, according to Paul Harrison, and our experience with the Chinese is in accord with his. Evidence is already available, in fact, that early rising may facilitate the healing of clean wounds.

CONCLUSIONS

The passing years have brought a change in the concept of surgical care. Surgery is emerging from the narrow circle of the barber surgeons and from

the belief that the great individual surgical technicians of the nineteenth and early twentieth century had given us the Golden Age of Surgery. The passing years have shown that teams of surgeons working as a group, each interested in science as a whole, but each becoming proficient in a special field, can do more to advance the borders of knowledge than can the individualist however skillful he may be.

Such a change in concept has resulted in an ever-increasing extension of surgical therapy to a wide variety of previously nearly hopeless disorders. It has led to a more radical approach to certain lesions and a more physiologic approach to others. It has led to a constantly decreasing morbidity and mortality of nearly all operations, and it has led to extensions in our knowledge of normal function and of the abnormalities which disease imposes upon normal function.

The surgeon of today is better equipped by training to evaluate the newer aids to therapy and to apply them. He appreciates the advantages of the newer anesthetics and their adjuncts and the value of trained medical personnel in administering them.

I repeat that the operation will probably always remain the most dramatic part of surgical therapeutics, but a successful operation now means a well patient who is restored to a useful place in society. The status of surgical therapy has changed and will continue to change to the end that patients previously denied operation will receive it and that the morbidity and mortality of operations will continue to decrease further and the end results continue to improve.

The science of surgery is in its infancy; even the art of surgery which Baron Boger 147 years ago said had reached the greatest heights to which it could ever attain is still to be expanded. If surgery is to remain a dynamic force in the medical sciences, it must constantly change as new knowledge becomes available. Surgeons, as well as all those who live and work in the field of experimental pathology, must be eager and willing to accept such changes. It was because of his facility to adjust so easily to the changing concepts of care that Judd was one of the distinguished surgeons of our time.

REFERENCES

1. Wangensteen, O. H., and Paine, J. R.: J. A. M. A. **101**: 1532, 1933.
2. Johnston, C. G., and Abbott, W. O.: Surg., Gynec. & Obst. **66**: 691, 1938.
3. Wangensteen, O. H.: Intestinal Obstruction, ed. 2, Springfield, Ill., 1942, Charles C Thomas, Publisher.
4. Abbott, W. O., and Johnston, C. G.: Surg., Gynec. & Obst. **66**: 691, 1938.
5. Whipple, O. H.: SURGERY **8**: 289, 1940.
6. Leigh, O. C., Jr., Nelson, J. A., and Swenson, P. C.: Ann. Surg. **111**: 186, 1940.
7. Mann, F.: J. A. M. A. **71**: 1184, 1918.
8. Cournand, A., Riley, R. L., Bradley, S. E., Breed, E. S., Noble, R. P., Lauson, H. D., Gregersen, M. I., and Richards, D. W.: SURGERY **13**: 964, 1943.
9. Frank, H. A., Seligman, A. M., and Fine, J.: J. Clin. Invest. **24**: 435, 1945.
10. Frank, H. A.: Personal Communication.
11. Anderson, D. P.: Ann. Surg. **108**: 918, 1938.
12. Carrel, A., and du Nöuy, P. L.: J. Exper. Med. **34**: 339, 1921.
13. Churchill, E. D.: Tr. Am. S. A. **62**: 268, 1944.
14. Cannon, P. R.: J. A. M. A. **128**: 360, 1945.
15. Kirby, C. K.: S Clin. North America, 1389-1403, 1946.
16. Van Jaseke, R. T.: Chirurg **9**: 274, 1937.

17. Zava, L.: Policlinico (sez. prat.) **47**: 865, 1940.
18. Leithauser, D. J.: Arch. Surg. **47**: 203, 1943.
19. Homans, John: New England J. Med. **211**: 993, 1934.
20. Allen, A. W.: Bull. New York Acad. Med. **22**: 169, 1946.
21. Murray, G. D. W., and Best, C. H.: Ann. Surg. **108**: 163, 1938.
22. Crafoord, C., and Jorpes, E.: J. A. M. A. **116**: 2831, 1941.
23. Varco, R. L.: SURGERY **19**: 303, 1946.
24. Keys, A., Taylor, H. L., Mickelsen, O., and Henschel, A.: Science **103**: 669, 1946.
25. Whipple, G.: Am. J. M. Sc. **203**: 477, 1942.
26. Cannon, P. R., Chase, W. E., and Wissler, R. W.: J. Immunol. **47**: 133, 1943.
27. Whipple, G. H., and Davis, N. C.: Arch. Int. Med. **27**: 679, 1921.
28. Ravdin, I. S., McNamee, H. G., Kamholz, J. H., and Rhoads, J. E.: Arch. Surg. **48**: 491, 1944.
29. Wolbach, S. B., and Howe, P. R.: Arch. Path. & Lab. Med. **1**: 1, 1926.
30. Lanman, T. H., and Ingalls, T. H.: Ann. Surg. **105**: 616, 1937.
31. Taffel, M., and Harvey, S. C.: Proc. Soc. Exper. Biol. & Med. **38**: 518, 1938.
32. Thompson, W. D., Ravdin, I. S., and Frank, I. L.: Arch. Surg. **36**: 500, 1938.
33. Munro, Donald: Personal Communication.
34. Mulholland, J. J., Co Tui, Wright, A. M., and Vinci, V. J.: Ann. Surg. **117**: 512, 1943.
35. Madden, S. C., and others: Surg., Gynec. & Obst. **82**: 131, 1946.
36. Koop, C. E., Riegel, C., Grigger, R. P., and Barnes, M. T.: Surg., Gynec. & Obst. **84**: 1065, 1947.
37. Ries, Emil: J. A. M. A. **33**: 454, 1899.

THE PATHOGENESIS OF DIASTOLIC HYPERTENSION

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INTRODUCTION

IN THIS paper physiologic knowledge pertinent to an understanding of kidney homeostasis is presented. In addition, a concept of the pathogenesis of diastolic hypertension is offered which has evolved from such knowledge and from studies of Cushing's syndrome. Previously evidence has been advanced to show that this syndrome may result from atrophic changes in the hypothalamic nuclei or their compression by increased intraventricular pressure with a resultant depression of the neural hypophysis, without the presence of tumors of the hypophysis, of the adrenal, of the thymus, or of the ovary (Heinbecker[1]). Diastolic hypertension with circulatory characteristics indistinguishable from those observed in persons with essential hypertension invariably exists in persons with the syndrome.

It is postulated now that functional influences in the central nervous system, particularly in the frontal lobes of the cerebral cortex, in those constitutionally susceptible may be of sufficient degree to depress the hypothalamic nuclei which control the neural hypophysis, to initiate changes in the glandular hypophysis, and thereby in other endocrine glands to cause the diastolic hypertension called "essential" with characteristics similar to those observed in persons with Cushing's syndrome, but without the development of all the other stigmas of the syndrome.

The anatomic basis for such influences on the hypothalamus is well established. On depression of the functional activity of its nuclei there results a diminution in the secretion of the neural hypophysis. One consequence of this is to cause a stimulation of the eosinophile cells of the glandular hypophysis, which have been shown to exercise a trophic effect on the heart, the renal tubules, and the adrenal gland. Another effect is to sensitize the blood vessels to the constricting action of epinephrine, of desoxycorticosterone, and of renin. Overaction of the desoxycorticosterone fraction of the adrenal cortical hormone effects a constriction of the efferent glomerular arterioles of the kidney and thereby leads to the release of renin. The combined action of all three substances here as in Cushing's syndrome is believed responsible principally for generalized arteriolar narrowing and the development of diastolic hypertension.

The sympathetic nervous system and epinephrine are considered to act in a manner which is qualitatively somewhat similar to the aforementioned, but their action is regarded as periodic and temporary to meet emergency bodily requirements (Heinbecker[2]).

Read at the thirty-third annual session of the American College of Surgeons, Sept. 11, 1947, New York, N. Y.

*Recipient of a grant-in-aid of research from the Commonwealth Fund.

THE SECRETION OF THE NEURAL HYPOPHYSIS AND ITS CONTROL

The secretion of the neural hypophysis is entirely under neurogenic control since denervation of the secretory cell-containing tissue results in complete cessation of secretion (Heinbecker, White, and Rolf[3]). Fibers to the neural hypophysis arise in two hypothalamic nuclei, the supraoptic and the paraventricular. All cells of the supraoptic nucleus send their fibers to the neural hypophysis, 70 to 80 per cent to the infundibular process, the remainder to the infundibulum. The inferior rostral portion of the paraventricular nucleus, representing 30 to 40 per cent of its cell content, sends fibers to the median eminence, few if any being distributed to the posterior lobe (Rasmussen,[4] Heinbecker and White[5]). The cells in the superior caudal portion of the nucleus

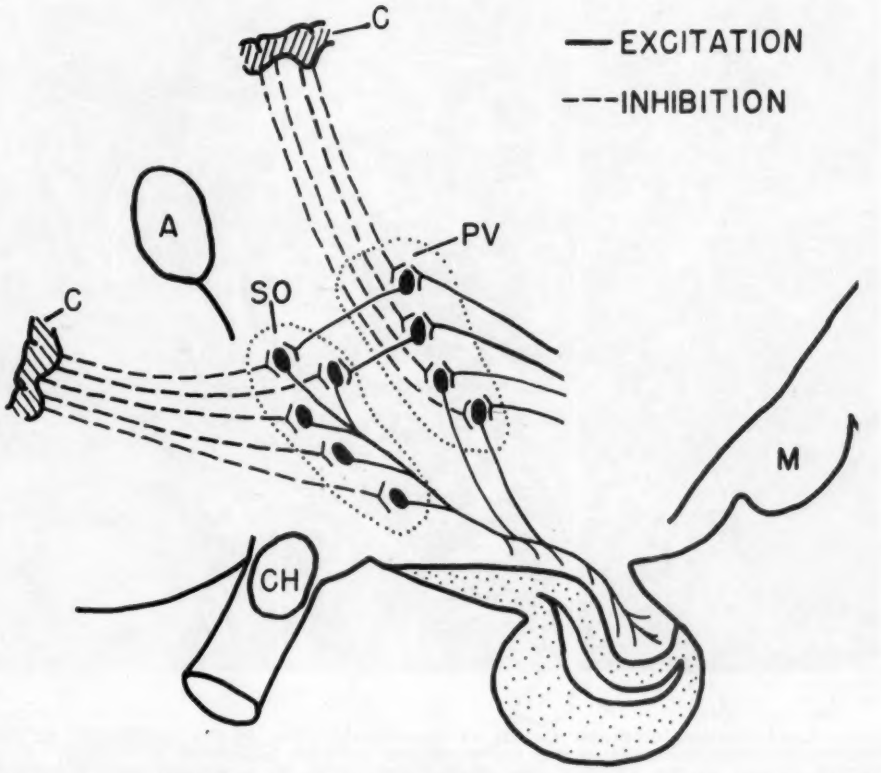


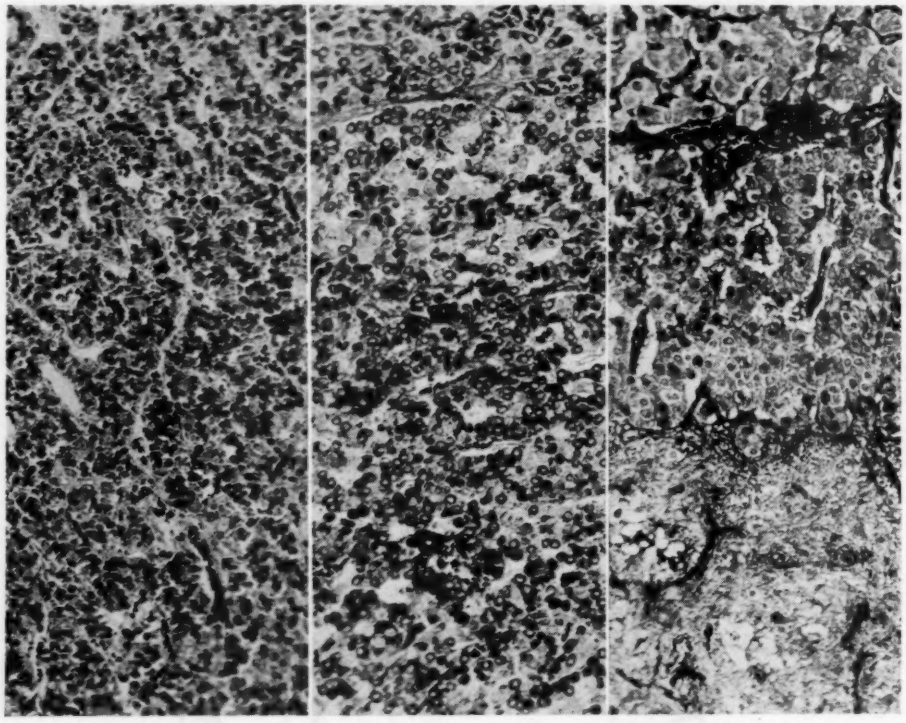
Fig. 1.—Schematic diagram of the innervation of the neural hypophysis. The manner in which the supraoptic (*SO*) and the paraventricular (*PV*) nuclei are interrelated and their activity subject to modification by influences from the cortex (*C*) and by afferent excitatory fibers to the paraventricular nucleus are indicated.

apparently send their fibers rostrally, not caudally, because following a puncture wound caudal to the stalk, between it and the mammillary bodies, the cells of the paraventricular nuclei do not show retrograde degeneration. When a lesion is made through the paraventricular nucleus the cells rostral to it degenerate. A lesion caudal to the paraventricular nuclei does not result in diabetes insipidus. This evidence supports the interpretation that fibers reaching the superior caudal portions of the paraventricular nucleus from below are afferent to the nucleus and exert an excitatory influence. Greving[6] has shown that the paraventricular nucleus is connected with the supraoptic nucleus by a chain of small cell groups

and by a fiber tract, presumably affording a mechanism for influences on the supraoptic nucleus by the paraventricular nucleus. The manner in which the supraoptic and paraventricular nuclei are interrelated and under influence from other parts of the nervous system is schematically shown in Fig. 1.

EFFECT OF SECRETION OF NEUROHYPOPHYSIS ON THE GLANDULAR HYPOPHYSIS

In dogs it has been shown repeatedly (Heinbecker[7]) that total denervation of the neural hypophysis results within three to five months in a complete loss of basophile cells, leaving only eosinophile and chromophobe cells (Fig. 2). It has been shown also that a lesion in the hypothalamus caudal to the stalk, so



A. *B.* *C.*

Fig. 2.—*A*, Photomicrograph (×135) of the anterior lobe of the hypophysis of puncture dog, type 1, showing eosinophiles and chromophobes with no basophiles remaining. *B*, Photomicrograph (×135) of the anterior lobe of the hypophysis of a normal female control dog. *C*, Photomicrograph (×135) of anterior lobe of hypophysis of dog six months after adrenalectomy. Dog maintained on four implanted pellets of desoxycorticosterone of 125 mg. each. Note the large basophile cells, many chromophobe cells, and a marked decrease in the number of eosinophile cells.

placed as to interrupt fibers caudal to the paired paraventricular nucleus, decreases the number and lessens the density of the granules in the nuclei of the remaining basophile cells. The eosinophile and chromophobe cells remain cytologically normal. The exogenous administration of 40 units of Pituitrin and 5 units of Pitressin tannate in oil daily for thirty days has resulted in an increase in basophile cells of the glandular hypophysis (Heinbecker[8]).

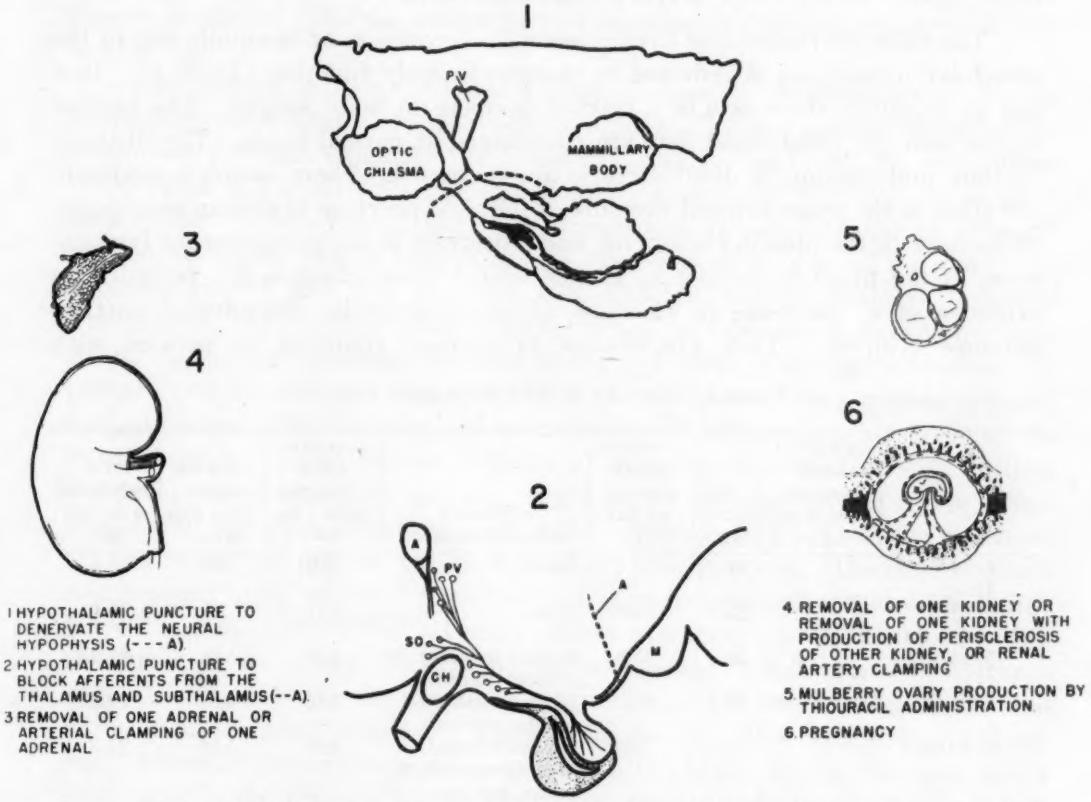
TARGET ORGANS OF HYPOPHYSIAL EOSINOPHILE HORMONE

Examination of the endocrine glands of female dogs whose neural hypophysis has been denervated reveals that the adrenal gland and the corpus luteum

do not atrophy. In male dogs the adrenal gland, the prostate, and the interstitial cells of the testis do not atrophy. In both the thyroid gland fails to develop colloid normally and the germ cells do not mature, due presumably to the absence of the basophile cells. It has been shown by us that in such dogs the kidney and the adrenal remaining after unilateral nephrectomy or adrenalectomy will hypertrophy to a normal or near normal degree (Heinbecker[9]).

EXPERIMENTAL PRODUCTION OF EOSINOPHILE CELL PREPONDERANCE WITH OVERACTION

Eosinophile cell preponderance has been produced experimentally in the dog in a number of ways (Fig. 3). It has been produced by total or partial denervation of the neurohypophysis. It has been produced also by the production of partial asphyxia of one adrenal gland according to the method described


1
PV
OPTIC CHIASMA
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A
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1 HYPOTHALAMIC PUNCTURE TO DENERVATE THE NEURAL HYPOPHYSIS (- - - A)
2 HYPOTHALAMIC PUNCTURE TO BLOCK AFFERENTS FROM THE THALAMUS AND SUBTHALAMUS (- - A)
3 REMOVAL OF ONE ADRENAL OR ARTERIAL CLAMPING OF ONE ADRENAL
4 REMOVAL OF ONE KIDNEY OR REMOVAL OF ONE KIDNEY WITH PRODUCTION OF PERISCLEROSIS OF OTHER KIDNEY, OR RENAL ARTERY CLAMPING
5 MULBERRY OVARY PRODUCTION BY THIOURACIL ADMINISTRATION
6 PREGNANCY

Fig. 3.—Chart to indicate the manner in which eosinophile cell preponderance with overaction has been produced experimentally in the dog.

by Victor.[10] In our experience definite diastolic hypertension is difficult to produce with any degree of regularity by this method. In two of three dogs the rise in mean pressure recorded through direct arterial puncture was 15 mm. Hg and in a third 30 mm. Hg. In the latter dog, serially cut 5 micron sections of the glandular hypophysis three months after the operation showed a definite eosinophile cell preponderance. In other experiments eosinophile cell preponderance was produced by wrapping a kidney in silk, the remaining kidney being

removed. The change in the cytology of the hypophysis was evident five to eight weeks after the renal wrapping. In four female dogs it was found after the administration of thiouracil 4 mg. daily for six months. In such animals there occurred mulberry ovaries. The corpora lutea were highly vascularized and showed large actively secreting cells. The hypophyses of such female dogs revealed an increase in basophile cells such as are found after thyroidectomy, but also many more large, highly granular eosinophile cells than were found in the hypophyses of the male dogs after similar drug administration. The hypophysis of dogs examined during gestation shows a marked preponderance of eosinophile cells.

EFFECT OF EOSINOPHILE CELL PREPONDERANCE ASSOCIATED WITH BASOPHILE DEPRESSION ON BODILY FUNCTIONS OF DOGS WITH THE NEURAL HYPOPHYSIS DENERVATED

The effect of eosinophile overaction with depression of basophile cell in the glandular hypophysis is reflected in changes in body function (Table I). In a dog so modified, there occurs a marked increase in body weight. The cardiac output and the renal blood flow are maintained at normal levels. The diodrast thulium and the inulin diodrast ratio are increased. There occurs a moderate elevation in the mean arterial pressure, a fourfold decrease in insulin sensitivity, an increase in the plasma cholesterol, and a decrease in the percentage of lymphocytes in the blood to as low as 12 per cent. These changes are regarded as evidence of an increase in function of the eosinophile cell-adrenal cortical hormone complex. They are similar to changes resulting in persons with

TABLE I. RESULTS ON PUNCTURE DOG, TYPE 1

DATE	MEAN BLOOD PRESSURE (MM. PER HG.)	WEIGHT (KG.)	AVERAGE URINE OUTPUT PER DAY (C.C.)	HORMONE ADMINISTRATION	D CLEARANCE (C.C. PER MIN. PER M²)	I CLEARANCE (C.C. PER MIN.)	D TM (MG. I PER MIN. PER M²)
12/30/40 Preop.		14		None	250	82	13.4
10/13/41 237 days P.O.		25.7	5500	None	251	85	13.3
5/14/42		34	6500	8 days anterior lobe extract	458	128	27.22
5/21/42		34.5		15 days anterior lobe extract	332	116	26.5
9/29/42		37	7000	8 days adrenal cortical extract, 8 c.c. per day	460	140	21.3
1/ 8/43 686 days P.O.		36.2	5600	None	462	129	18.6
3/26/43	136	38	5500	None	306	100	28.96
3/ 6/44		35.9	4900	None	338	86	25.67
3/31/44		37	4000	8 days adrenal cortical extract, 8 c.c. per day	411	105	27.86
11/23/45 4 yr. 9 mo. P.O.		43.5	4800	None	261	110	23.44
12/ 7/45	140	43.5	4800	9 days doca, 4 mg. per day	268	110	25.3
12/20/45	160	43.5	5900	9 days doca, 12 mg. per day	240	163	26.1

Cushing's syndrome, whether due to an adrenal cortical tumor or to hypothalamic nuclear depression through atrophy or increased intracranial pressure (Heinbecker[11]).

In contrast a marked decrease of eosinophile cells in the hypophysis is associated with weight loss and a low blood pressure (Fig. 2).

SENSITIZATION TO EPINEPHRINE, TO RENIN, AND TO DESOXYCORTICOSTERONE

It has been found that a loss of the secretion of the neural hypophysis produces other effects which are significant in the problem of the pathogenesis of diastolic hypertension. These are a sensitization to epinephrine, to renin, and to desoxycorticosterone.

Sensitization to Epinephrine.—The evidence in support of the sensitization to epinephrine has been previously reported (Heinbecker[12]). The sensitization is considered to be due primarily to a decrease in the secretion of the neural hypophysis.

Sensitization to Renin.—Three groups of dogs are reported upon. In one group thirty were totally hypophysectomized, in another six were simply hypophysectomized (median eminence not removed), and in the third, five were punctured (type 1, Fig. 4). Attempts were made to wrap one kidney in the dogs of each group. It was found that such a procedure invariably resulted in death from shock within twenty-four to seventy-two hours of the dogs of the totally hypophysectomized and the puncture groups when marked diabetes insipidus was present. In the dogs which died there was no evidence of marked nitrogen retention, the highest recorded being 66 mg. per cent. The dogs recovered completely from the anesthetic and for twelve to twenty-four hours were apparently normal, eating and drinking. It was after this that they developed the symptoms of shock. There was no evidence of hypoglycemia or of adrenal cortical deficiency as evidenced by changes in the serum sodium and the serum potassium. The blood pressure fluctuated widely from slightly hypotensive values at the beginning to final low values such as are seen in shock. The state of shock was brought about chiefly by marked loss of plasma and of red blood cells into the walls of the gastrointestinal tract. There was always much free blood within the lumen of the bowel. The regions of most marked swelling and hemorrhage were the stomach, the duodenum, the jejunum, the lower ileum, and the first portions of the large intestine. The skeletal muscles often were dry and bloodless. Petechial hemorrhages were present in the brain, in the pancreas, in the liver, and in the lungs. The kidneys were grossly and microscopically intact, except for some enlargement of the wrapped kidney. These findings are identical with those which follow the clamping of both renal arteries so markedly as to result in rapid death of the animal (Goldblatt[13]). Dogs simply hypophysectomized stood the procedure of wrapping a kidney with some degree of depression, but after recovery the remaining kidney could be removed safely. Such dogs then went on to develop hypertension and in six to nine months uremia and death. The fact that simply hypophysectomized dogs permit the kidney wrapping indicates that it was not the loss of the glandular hypophysis which led to the sensitization to renin in the totally hypophysectomized dogs

Removal of one kidney could be successfully carried out in all three types of dog, indicating that the substance leading to the shock was released from the wrapped kidney.

From these experiments it is concluded that marked loss of the secretion of the neural hypophysis sensitizes a dog to a substance released from a wrapped kidney. Loss of the anterior lobe per se does not sensitize the dog to this substance. Kohlstadt, Helmer, and Page[14] and other investigators have demonstrated that, following the wrapping of a kidney, the substance released can be identified as renin. There seems no a priori reason to doubt that it also was the substance released in our dogs. The amount released from the wrapping of a

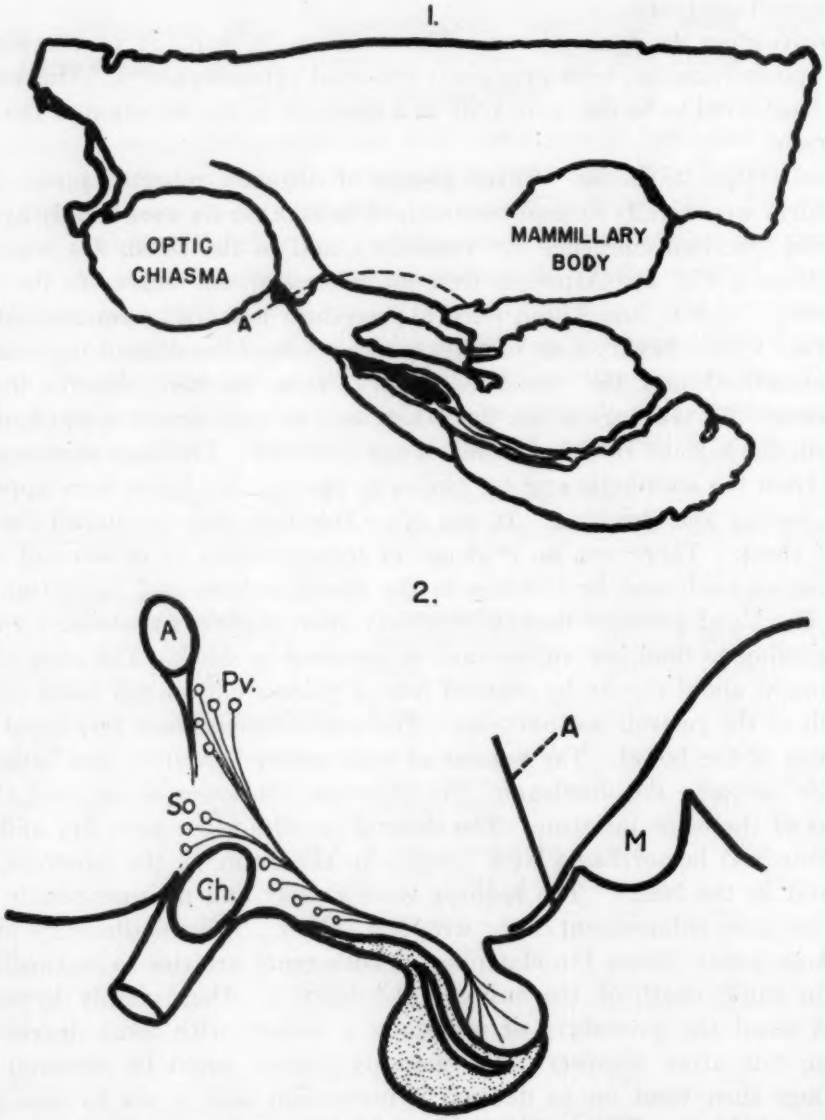

Fig. 4.—*1*, Diagram to indicate the site of the lesion (*A*) whereby the neural division of the hypophysis is severed from the supraoptic and the paraventricular nuclei. A dog so prepared is referred to as a puncture dog, type 1. *2*, Diagram to indicate the site of the lesion (*A*) for severing fibers afferent to the paired paraventricular nucleus. Such a dog is referred to as a puncture dog, type 2.

single kidney within twenty-four to seventy-two hours with the remaining kidney normal is assumed to be similar to that released when one kidney is wrapped in a normal dog, in which it is not sufficient to precipitate any untoward symptoms. The fact that death follows the procedure in dogs when the secretion of the neural hypophysis is lacking is interpreted as indicating that it is the absence of this secretion which sensitizes to renin.

Sensitization to Desoxycorticosterone.—It has been observed repeatedly in man and shown in the dog (White, Heinbecker, and Rolf[15]) that adrenal cortical deficiency results in an increased responsiveness of the blood vessels to the vasoconstricting action of desoxycorticosterone. Investigation in the dog with the neural hypophysis denervated but with the glandular hypophysis left intact reveals an increased sensitivity to the constricting action of desoxycorticosterone on the efferent glomerular arterioles as indicated by an increased filtration fraction greater than is customarily exhibited by normal dogs (Table II).

TABLE II. EFFECT OF NEURAL HYPOPHYSIAL DENERVATION (PUNCTURE TYPE 1) ON SENSITIVITY TO DESOXYCORTICOSTERONE AS INDICATED BY ALTERATION IN THE FILTRATION FRACTION*

REMARKS	D OR PAH CLEARANCE (C.C. PER MIN. PER M²)	INULIN PLASMA CLEARANCE (C.C. PER MIN. PER M²)	FILTRATION FRACTION
Dog K35			
Normal	279	87	.31
4 pellets (125 mg. each) desoxycorticosterone implanted 14 days previously	262	83.3	.32
6 mg. Doca per day for 6 days	270	90.9	.34
No extract for two days			
6 mg. Doca, 150 units Preloban per day for 5 days	345	120.7	.35
Dog X27			
127 days after puncture	237	73.3	.31
10 mg. Doca per day for 7 days	283	117.5	.42
Dog K18			
Normal	250	82	.32
4 yr. 9 mo. after puncture operation; no extract	261	110	.42
Doca, 4 mg. per day for 9 days	268	110	.41
Doca, 10 mg. per day for 9 days	240	163	.68

*Results of D or PAH and I clearances after the administration of desoxycorticosterone to a normal and to two puncture dogs, type 1.

EFFECT OF GLANDULAR HYPOPHYSIS ON CARDIAC OUTPUT AND RENAL TUBULAR FUNCTION

In other experiments (White, Heinbecker and Rolf[16]) it has been shown that in the dog hypophysectomy results in a marked decrease in cardiac output which is manifested within one week and may reach 50 per cent in four to six weeks. At this time the decrease in basal metabolic rate averages 30 per cent. The administration of exogenous anterior pituitary extract can be made to restore to normal or above the cardiac output of hypophysectomized dogs.

From the results of these experiments, it is concluded that the decrease in renal blood flow following hypophysectomy is to be attributed to a decrease in

cardiac output rather than to any specific influences on the kidney blood vessels. Such a decrease in cardiac output does not occur in the dog with the neural hypophysis denervated and in which all basophiles in the glandular hypophysis disappear. This is reflected in the maintained renal blood flow in the dogs. From such evidence it is concluded that it is the loss of eosinophiles which is responsible essentially for the decrease in cardiac output following hypophysectomy.

After hypophysectomy the decrease in the capacity of the renal tubules to transport diodrast at high plasma levels always has been found greater than the decrease in renal plasma flow (Heinbecker, White, and Rolf[17]). It is held, therefore, that the eosinophile cells of the hypophysis exercise a direct trophic influence on renal tubular function.

EFFECT OF EXOGENOUS DESOXYCORTICOSTERONE AND OF RENIN ON URINE EXTRACT

In this laboratory, large doses of desoxycorticosterone (6 to 10 mg. daily) have been administered to totally hypophysectomized dogs with a resultant increase in urine output. Similar experiments in which even larger doses were administered to normal dogs with similar results had previously been reported by Ragan and associates[18] and by Mulinos and co-workers.[19] Such experimental results support the view that this hormone has certain effects which are antagonistic to those of the secretion of the neural hypophysis.

Experiments to show the effect of relatively large doses of intravenously administered exogenous renin on the blood pressure and the urine output of rabbits have been reported by Pickering and Prinzmetal.[20] These investigations have demonstrated adequately that a substance extracted from the kidney which has pressor effects and which is considered by them to be renin, also has a diuretic effect in the unanesthetized rabbit. The threshold for the pressor effect is considerably lower than the threshold for diuresis. The chloride content of the urine during the diuretic phase rises toward that of plasma. These investigators attribute the diuretic action of renin to an inhibition of the reabsorption of water, of sodium, and of chloride by the renal tubule cells.

THE EFFECT OF EPINEPHRINE, OF DESOXYCORTICOSTERONE, AND OF RENIN ON THE DYNAMICS OF RENAL BLOOD FLOW

The effect of exogenous epinephrine on renal blood flow has been studied by Smith.[21] He has demonstrated that in lesser concentrations it causes a narrowing of the efferent glomerular arterioles and in stronger concentration a significant decrease in renal blood flow, which is interpreted as indicating also a narrowing of the afferent glomerular arterioles.

The effect of exogenous desoxycorticosterone on renal circulation in the normal and in the dog with the neural hypophysis denervated has been investigated in this laboratory. A first effect is a narrowing of the efferent glomerular arterioles; then in higher concentrations there presumably is also some narrowing of the afferent arterioles as evidenced by a slight diminution in the circulation through the kidney as a whole. With the narrowing of the afferent arterioles there occurs a significant rise in systemic mean arterial pressure.

The effect of exogenous renin on blood flow through the kidney has been studied among others by Corcoran, Kohlstadt, and Page,[22] and by Goldring, Chasis, Ranges, and Smith.[23] Its ultimate effect is similar to that of epinephrine and of desoxycorticosterone.

RENIN IN RELATION TO HYPERTENSION

That diastolic hypertension may arise from factors primary in the kidney has been established by Tigerstedt and Bergman,[24] by Goldblatt and associates,[25] and by Braun-Menendez and co-workers.[26] It is not deemed necessary to review in detail the renin mechanism for hypertension, as this has been done recently by others (Pickering[27a]). The conclusion may be accepted that the kidney under conditions of altered hemodynamics releases renin, which working on a globulin substrate results in the production of a pressor substance, angiotonin, or hypertension. The circulation in animals made hypertensive by renin is similar in many respects to the circulation in persons with essential hypertension.

On the basis of evidence submitted in this report and that of other investigators in this field, it is believed that the factors responsible for the release of renin are those which cause a decrease in the amount of effective renal tubular tissue. This may result from a narrowing of the glomerular arterioles or of the larger arteries to the kidney or of both. The final effect is the lessening of the circulation to the renal tubules considered to be the source of renin. Known factors capable of modifying the dynamics of the renal circulation in this manner are the vasomotor nerves, epinephrine, and the desoxycorticosterone fraction of the adrenal cortical hormone. In addition to such nervous and humoral influences, there develop in man occlusive changes in the walls of the renal blood vessels themselves both in response to the hypertension and because of metabolic disturbances initiated by the very endocrine imbalances responsible for the functional arteriolar narrowing.

The decrease in effective renal tubular tissue may be brought about also by removal of one kidney. Following this, there results a preponderance and stimulation of the eosinophile cells of the glandular hypophysis and an enlargement of the adrenal glands. A similar change in the cytology of the glandular hypophysis follows the wrapping of one kidney with silk, the other being left intact. There occurs early also a definite hypertrophy of the unwrapped kidney and even of the wrapped kidney if the silk is loose enough to permit the expansion (Heinbecker[27b]). Inasmuch as it has been established that the wrapping of a kidney leads to the release of renin, it is assumed that the stimulation of the hypophysial eosinophile cells is due to the direct or indirect action of renin. Other things being unchanged, the overaction of the eosinophile-adrenal cortical hormone complex undoubtedly would cause some increase in cardiac output, and thus of general blood flow. Because the hypertrophy is confined essentially to the remaining unwrapped kidney, it follows that this kidney must receive a greater than normal fraction of the total cardiac output during its period of developing hypertrophy. Because a similar degree of hypertrophy does not occur in the absence of the glandular hypophysis and because the glandular hypophysis does not exert its influence on the kidney circulation in

the absence of adrenal cortical hormone, it is postulated that the combined action of an eosinophile cell-desoxycorticosterone-renin hormone complex is to increase the blood supply of the remaining kidney to permit its hypertrophy. When the normal amount of renal tubular tissue has been restored, the release of renin ceases.

PROGESTERONE AND DIASTOLIC HYPERTENSION

Structurally, progesterone is related closely to desoxycorticosterone. Its hormonal similarity has been established in various ways. Thus, Gaunt and Hays[28] showed that its administration aids in keeping adrenalectomized ferrets alive. McKeown and Spurrell[29] proved the life of adrenalectomized rats is prolonged in pregnancy. Thorn and Engel[30] have shown that sodium retention and a slight decrease in urine output follow its administration.

Progesterone renders the uterine musculature insensitive to Pituitrin (Reynolds and Allen[31]). This accounts for the failure of the uterus of the pregnant rabbit to respond to Pituitrin (Knaus[32]). It suggests that the eosinophile cell preponderance in the hypophysis of pregnancy may result from such insensitivity to Pituitrin because the absence of Pituitrin has been shown to result in eosinophile cell preponderance and a loss of basophile cells in the dog. The adrenal hypertrophy associated with pregnancy could be attributed to such eosinophile cell preponderance because of the trophic relationship of these cells to the adrenal cortex.

In the case of Cushing's syndrome associated with an ovarian tumor reported by Norris,[33] it is assumed that the hormone secreted by the tumor was progesterone rather than estrogen because Zondek[34] has shown that large amounts of estrogenic substances depress the eosinophile but not the basophile cells. In the case reported by Norris the eosinophile cells were normal, whereas the basophile cells showed degranulation as in all other cases of Cushing's syndrome. The patient in Norris' case exhibited diastolic hypertension and arteriosclerosis.

It would be anticipated, then, that in pregnancy progesterone might exert an influence similar to that of desoxycorticosterone on the blood vessels.* Sensitization to progesterone would be expected to follow from its neutralizing influence on the secretion of the neural hypophysis.

DIASTOLIC HYPERTENSION IN PERSONS EXHIBITING CUSHING'S SYNDROME

Evidence has been presented (Heinbecker,[35, 36]) that the primary cause of Cushing's syndrome may be (1) an adrenal cortical tumor, (2) a tumor of the ovary, or (3) a tumor of the thymus. In a group of cases without any primary tumor it has been shown (4) that the initiating cause may be a depression of the paraventricular nuclei of the hypothalamus and, to a lesser degree, of other hypothalamic nuclei, particularly the supraoptic. This depression was due in five cases to an actual atrophy of the nuclear cells but in one instance was shown to be functional because recovery occurred on release of an increased intraventricular pressure on removal of a meningioma at the foramen magnum. In

*It has been reported by M. L. Goldman and H. A. Schroeder in the Federation Proceedings of the American Physiological Society, March, 1948, that the intravenous injection of 5 mg. of progesterone in 2.5 c.c. of propylene glycol in persons with essential hypertension was followed by an elevation in blood pressure.

the five cases in which atrophy of the nuclei was found, the flattened ependymal lining of enlarged ventricles indicated that pressure could have been responsible for the atrophic changes. In two early recent cases of Cushing's syndrome the intraventricular pressure was measured and found to be twice the normal. These observations suggest the possibility that an alteration in the hemodynamics of the intraventricular circulation in the tela choroidea similar to that involving the vessels of the face might be responsible for the increased intraventricular pressure.

All primary causes invariably lead to a degranulation or hyalinization of the basophile cells of the hypophysis as described by Crooke.[37] Evidence was presented to support the interpretation that when the primary cause is a tumor, its secretion may directly or indirectly have the capacity to neutralize the effectiveness of the secretion of the neural hypophysis. This brings about the same depression of the maturation of basophile cells with stimulation of eosinophile cell maturation as does a decrease of the secretion of the neural hypophysis when due to a depression of the function of hypothalamic nuclei which control its secretion. The signs and symptoms of Cushing's syndrome are such as to indicate that in this disease process the eosinophile cells are polyvalent in their trophic influence, as the adrenal cortical function is altered in relation to salt and water balance, and to metabolic and to androgenic functions. Diastolic hypertension with circulatory characteristics similar to those exhibited by persons with essential hypertension invariably develops. Arteriosclerosis indistinguishable in its nature and distribution from that seen in persons with essential hypertension also occurs. In cases of Cushing's syndrome not associated with primary tumors, the overaction of the eosinophiles is responsible for the initiation of changes leading to hypertension primarily through its stimulation of the adrenal cortex. In persons whose blood vessels, because of constitutional factors, are sensitized to the constricting action of its desoxycorticosterone fraction, generalized arteriolar narrowing as well as constriction of the efferent glomerular arterioles is effected. Constriction of the latter arterioles would be expected to result in the release of renin. On the basis of our experimental findings, such persons would be sensitized to renin, to desoxycorticosterone, and to epinephrine to the degree to which the secretion of the neural hypophysis is decreased or rendered ineffective. The overaction of the metabolic fraction of the adrenal cortical hormone, because of its influence on the metabolism of neutral fat and cholesterol, presumably leads to the infiltration of the walls of the arterioles with these substances and thereby to the development of arteriosclerosis, which makes the hypertension permanent (Heinbecker, White, and Rolf[38]).

A schematic diagram of the mechanism of development of the endocrine disturbances which lead to diastolic hypertension in Cushing's syndrome when the primary lesion is a depression of the hypothalamic nuclei is shown in Fig. 5.

DISCUSSION

Experimental and clinicopathologic evidence has been presented which now will be utilized to outline a homeostatic mechanism of which the kidney is

the focus (Fig. 6). The mechanism involves the interaction of the nervous system and the endocrine glands on the kidney. Its function is to maintain the adequacy of kidney filtration and kidney tubular function. This is accomplished whenever necessary by narrowing the caliber of the extrarenal and the efferent glomerular arterioles with a concomitant stimulation of the heart to maintain the cardiac output within the normal range. Direct stimulation of renal tubular cells also is involved. Pathologic processes in the nervous system, in the endocrine glands, and in the kidney may disturb the quantitative relationships of the

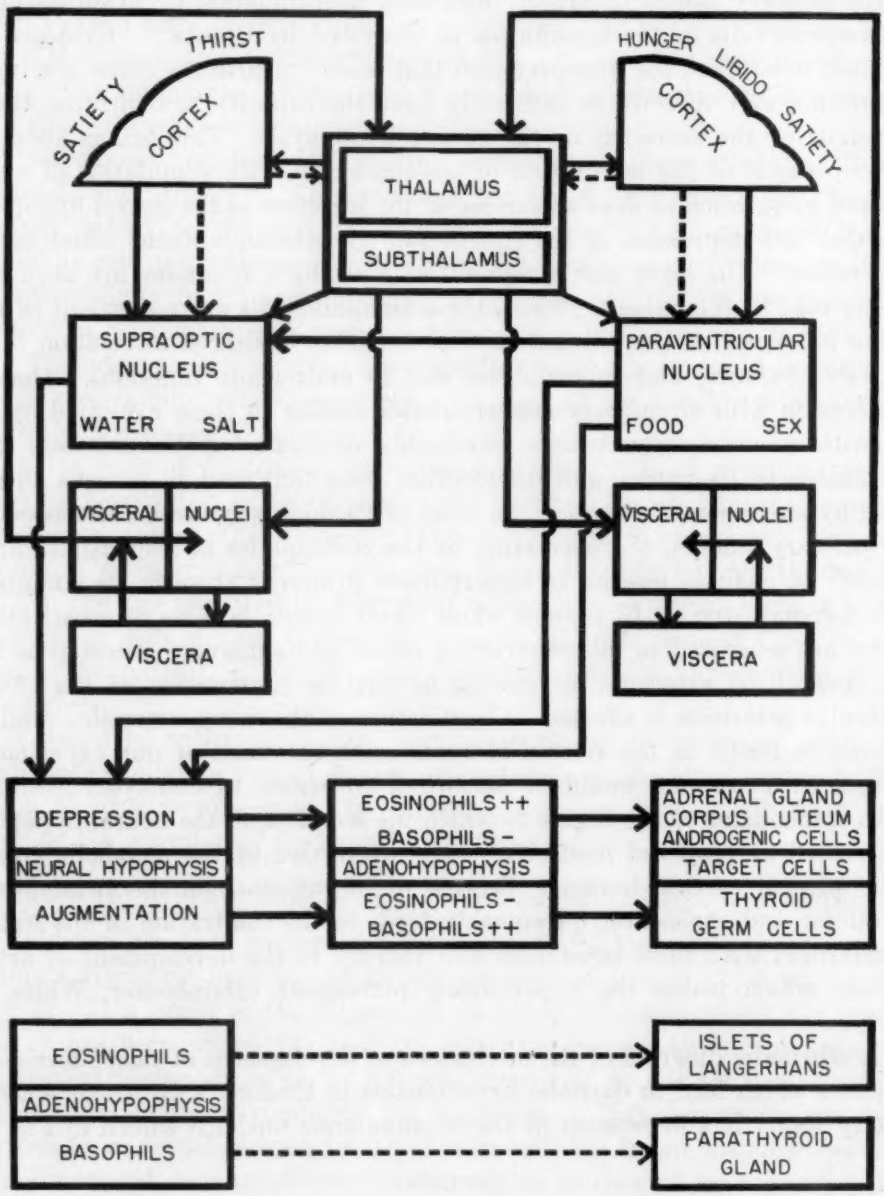

Fig. 5.—Diagram to indicate nervous system and glandular interrelationships in the production of Cushing's syndrome due to a primary lesion in the hypothalamus. (⟶ excitatory, - - - - → inhibitory influences.)

mechanism to result in diastolic hypertension. Depending upon which of the primary components of the mechanism the pathologic process involves, the associated signs and symptoms may vary. Whenever much derangement causes renal tubular inadequacy the secretion of renin is invoked to compensate by the induction of diastolic hypertension. It is assumed that in constitutionally susceptible persons the mechanism may be deranged through functional influences

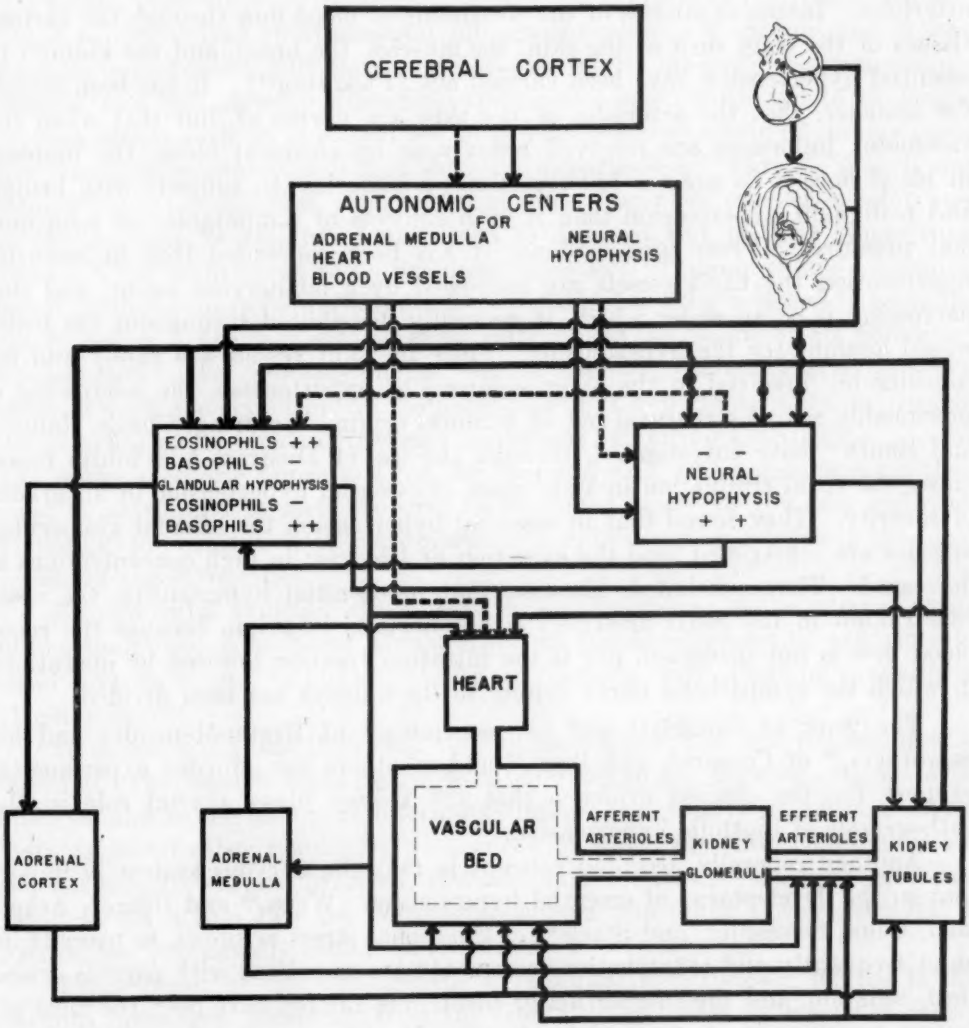

Fig. 6.—Schematic diagram to indicate the manner in which kidney function may be modified through nervous and endocrine influences. Straight ——— lines indicate excitatory, broken - - - - lines inhibitory influences; dotted straight .—.—.—. lines indicate neutralization of one influence by another. A decrease in the amount of or a depression of the functional influence of the secretion of the neural hypophysis together with other influences from the adrenal cortex, from renin and from progesterone, leads to overaction of the eosinophile cells of the glandular hypophysis. The existence of a differential susceptibility of the afferent and the efferent glomerular arterioles to vasoconstrictor influences affords a mechanism for modifying filtration by the glomeruli and by alterations in blood pressure to control the blood flow to the renal tubules whereby the adequacy of kidney function is maintained.

The excess release of a vasoconstrictor substance from the adrenal cortex, from the adrenal medulla, of renin from the kidney, or of progesterone from the ovary and placenta may lead to diastolic hypertension. In persons exhibiting Cushing's syndrome, destruction of the nuclei of the hypothalamus which are trophic to the neural hypophysis results in glandular imbalance which leads to hypertension. It is postulated that a functional depression of these nuclei by influences from the central nervous system leads, in those constitutionally susceptible, to similar glandular imbalances and to essential hypertension.

not associated with cytologically demonstrable changes in the nervous component to cause renal tubular inadequacy. Under such conditions the hypertension necessary to overcome it is spoken of as essential.*

Studies of the circulation in essential hypertension have shown that the raised arterial pressure is not due to an increased cardiac output or to increased blood viscosity, for these have been measured and found normal. It is recognized that diastolic hypertension is due to narrowing of the small arteries and arterioles. Intensive studies of the conditions of blood flow through the various tissues of the body such as the skin, the muscles, the brain, and the kidneys in essential hypertension have been carried out (Pickering[39]). It has been found, for instance, that the arterioles of the skin are narrowed, but that when the vasomotor influences are removed reflexly or by chemical block, the increase in blood flow is no greater but sometimes a little less in subjects with benign and malignant hypertension than it is in subjects of comparable age with normal pressures. From such evidence it has been concluded that in essential hypertension the hand vessels are narrowed by a nonnervous agent, and this narrowing is of an order which, if generally distributed throughout the body, would account for the hypertension. Since the skin vessels are rarely and inconsiderably involved in the arteriosclerosis of hypertension, the narrowing is presumably not of structural but of humoral origin. Goldring, Chasis, Ranges, and Smith[40] have investigated, through the use of Diodrast and inulin clearances, the renal circulation in sixty cases of essential hypertension of all grades of severity. They found that in essential hypertension the efferent glomerular arteries are constricted, and the excretion of Diodrast in high concentrations is decreased. They concluded, likewise, that in essential hypertension the vasoconstriction in the renal arterioles is not nervous in origin because the renal blood flow is not increased, nor is the filtration fraction lowered by operations in which the sympathetic nerve supply to the kidneys has been divided.

The work of Goldblatt and his associates,[41] of Braun-Menendez and his co-workers,[42] of Corcoran and Page,[43] and of others has afforded experimental support for the clinical evidence that the kidney plays a vital role in the pathogenesis of diastolic hypertension.

Another generally accepted concept is that the nervous system is important in the development of essential hypertension (Weiss,[44] and Binger, Ackerman, Cohn, Schroeder, and Steele[45]). Emotional stress is known to precede its onset frequently and exacerbations commonly are associated with psychic crises. Rest, sedation, and the elimination of disturbing factors have been the most effective measures in its medical treatment. However, as stated by Binger and his associates, in the present state of our knowledge, methods are not available to test the question of causation in the dynamic interrelationship of psyche and soma. It is also to be admitted that not all who exhibit diastolic hypertension give a recognizable evidence of psychic complex and not all who do have some

*Simultaneously with the presentation of this paper at the meeting of the American College of Surgeons in New York in September, 1947, it was learned that a sensitization of the blood vessels of patients exhibiting essential hypertension to the vasoconstricting action of desoxycorticosterone has been demonstrated by George A. Perera and David W. Blood (Ann. Int. Med. 27: 401, 1947). This is considered crucial support of the concept of the mechanism of the pathogenesis of essential hypertension herein presented.

psychic disturbance develop hypertension. Psychic influences have been shown to cause efferent glomerular arteriolar narrowing, and even to decrease the total renal blood flow of man (Smith[46]). Such effects have been observed by us repeatedly in the dog. An invariable and striking effect of the disturbing conditions has been to decrease Diodrast excretion. This depression of tubular function is regarded as a stimulus for the further release of renin now considered to be produced by the renal tubules (Friedman and Kaplan[47]).

It has been observed repeatedly that when a group of individuals is subjected to disquieting environmental influences such as are encountered in war, diastolic hypertension will develop in some but not in others, just as emotionally instable rats will develop diastolic hypertension when subjected to prolonged nervous strain such as is caused by noisy blasts, whereas rats of similar breed but emotionally stable will not develop hypertension (Farris, Yeakel, and Medoff[48]). An analogous experiment in effect has been carried out for man on the African Negro when transported to America and on the Chinese rural dweller when transferred to an urban environment. In both groups a constitutional tendency to develop diastolic hypertension has been revealed in some but not in others. The tendency is genetically linked, as shown by its hereditary transmission. The emphasis on the concept that hyperdynamic responsiveness of blood vessels is significant in the pathogenesis of hypertension is supported by the evidence of its constant presence in persons exhibiting Cushing's syndrome. The dusky plethoric appearance of the face and neck which distinguishes them must be attributed to such property in the blood vessels of the face and neck. Similarly, the exhibition of cutis marmorata indicates its existence in the blood vessels of the extremities.

Experimental evidence also attests to the importance of the adrenal cortex in the maintenance of blood pressure and in the development of experimental renal hypertension (Goldblatt[49]) and in persons with Cushing's syndrome (Heinbecker[50]).

It appears obvious then that any tenable concept of the pathogenesis of essential hypertension must assign essential roles to the nervous system, to the kidneys, and to the glands of internal secretion, particularly the adrenal cortex. Here as in all other regulatory phenomena in which the endocrine glands and the nervous system are involved, two factors play a role—one neurogenic and rapid in its action like the constrictor nerves, the other slower, humoral in nature, but functionally similar in its effects.

The concept of the pathogenesis of essential hypertension offered is that nervous influences, primarily from the frontal lobes, effect a functional depression of the supraoptic and paraventricular nuclei of the hypothalamus. Such depression may become organic as well if the intraventricular pressure becomes sufficiently elevated to exert actual pressure on the nuclei as it may in the malignant phase. The depression results in a decrease of the secretion of the neural hypophysis because of which the eosinophile cells of the glandular hypophysis become preponderant and are stimulated to overaction. The basophile cells are depressed. In persons with essential hypertension the stimulation of the eosinophiles and depression of the basophiles are presumably functional, as no obvious

organic changes have been recorded (Rasmussen[51a, b]). This change in the glandular hypophysis is the result of humoral action, not of nervous influences. Overaction of the eosinophile cells increases their output of adrenotropic hormone. One effect of the overaction of the adrenal cortex is to constrict the efferent glomerular arterioles of the kidney which in turn results in a release of renin. The combined influences of the hypophysial, of the adrenal cortical, and renal hormones also result in a constriction of the extrarenal blood vessels and in a maintained cardiac output, thereby causing diastolic hypertension. The processes involved are of a low order of intensity in most instances, as indicated by the fact that about fifteen to thirty years are required for essential hypertension to become well established. Doubtless a lesser concentration of the humors can be effective because the depression of the neural hypophysis sensitizes the blood vessels to the constrictive action of the desoxycorticosterone fraction of the adrenal cortical hormone, to epinephrine, and to renin. In addition, persons developing essential hypertension are considered constitutionally susceptible to the depression of both their hypothalamic nuclei by nervous influences and their blood vessels to the constrictive action of the hormones concerned in the development of hypertension. This is postulated because not all persons with diabetes insipidus develop essential hypertension. It might be expected that persons with diabetes insipidus would develop diastolic hypertension because of the marked depression of the secretion of the neural hypophysis which exists invariably. An analysis from the records of thirteen consecutive recent patients with diabetes insipidus admitted to Barnes Hospital reveals that in five of the thirteen a diastolic pressure of over 100 mm. of mercury was recorded. This is a much higher incidence of elevated diastolic pressure than occurs in persons generally. It is postulated that others with diabetes insipidus who do not develop hypertension do not have sufficient constitutional susceptibility of the blood vessels to vasoconstrictor hormones. In some persons with diabetes insipidus, injury to the glandular hypophysis is present also. Any such deficiency would diminish its adrenotropic influence and in this way militate against the development of essential hypertension.

The overaction of the eosinophile-adrenal cortical hormone complex is responsible for the excessive infiltration of neutral fats and of cholesterol into the walls of the blood vessels. This is considered of primary significance in the development of arteriosclerosis. It is the development of such sclerosis which makes the hypertension permanent.

Hypertension is regarded as the reaction of the body to any inadequacy of renal tubular function. It is part of the mechanism for compensating, with increased blood flow, the inadequacy of the renal tubules. Renin is regarded as the substance released by the kidney tubules, which not only constricts vessels outside the kidney directly, but also stimulates the eosinophiles of the glandular hypophysis, thereby increasing the cardiac output and renal tubular function. Slight excess of desoxycorticosterone, of renin, and of epinephrine causes constriction of the efferent glomerular arterioles, but the failure of the blood vessels to the renal tubules themselves to be damaged by an excess of renin in experimental renal hypertension permits the interpretation that they are not similarly affected.

In pregnancy the preponderance of eosinophile cells is regarded as the result of the inactivation of the secretion of the neural hypophysis by progesterone. The eosinophile cell overaction here as elsewhere stimulates the adrenal glands and in those emotionally and constitutionally susceptible would be expected to result in sufficient constriction of the efferent glomerular arterioles to release renin. As in essential hypertension, the combined action of these three hormones on vessels sensitized by depression of the neural hypophysis is regarded as primarily responsible for the initiation of the diastolic hypertension.

In support of the concept is the frequent association of obesity (Terry[52]), of hypercholesterolemia (Westphal[53]), of decreased sugar tolerance (Joslin[54]), of accelerated ageing and of the menopause (Alvarez and Zimmermann[55]) with the existence of essential hypertension. In the experimental animal, eosinophile adrenal overaction has been shown to be associated with obesity, with hypercholesterolemia, with a decreased insulin sensitivity, and with a failure of the ovarian follicles or of the spermatogonia to maturate (Heinbecker[56]). In Cushing's syndrome in which the mechanism for the development of hypertension seems similar to that postulated for essential hypertension, obesity, hypercholesterolemia, decreased insulin sensitivity, marked acceleration of the ageing processes, and depression of gonadal function are constant features (Heinbecker[57]). In persons with essential hypertension these signs often are not pronounced; they even may be absent. Such variations are attributed to differences in organ susceptibility to the common influences which impinge on them.

SUMMARY

Experimental evidence pertinent to the problem of pathogenesis of diastolic hypertension is reviewed.

Denervation of the neural hypophysis in the dog results in a loss of basophile cells and a preponderance with overaction of eosinophile cells in the glandular hypophysis.

With marked depression of the secretion of the neural hypophysis in the dog a normal cardiac output is maintained, the insulin-Diodrast clearance ratio increases, and a moderate elevation in mean arterial pressure develops.

Eosinophile cell preponderance and overaction in the dog also develop when the nervous pathways from the thalamus and subthalamus to the paraventricular and supraoptic nuclei are interrupted, when asphyxia in one adrenal gland is produced by ligation of a portion of its arterial supply, when a diminution in the amount of effective renal tubular tissue is produced by removal of one kidney with the wrapping of the remaining kidney in silk, when mulberry-like ovaries are produced by the prolonged administration of thiouracil, and when pregnancy occurs. Since several of these associated conditions result in development of diastolic hypertension, their common factor of eosinophile overaction is considered to be significant as a causative factor in the development of hypertension.

The eosinophile cells of the glandular hypophysis are trophic to the adrenal gland, to the renal tubules, and to the interstitial tissue of the gonads.

Loss or depression of the secretion of the neural hypophysis results in a sensitization of the blood vessels to epinephrine, to desoxycorticosterone, and

to renin. Under the conditions where depression of the neural hypophysis causes and induces increased output of the latter two of these hormones, the blood vessels are also sensitized to overaction and hypertension results.

In persons exhibiting Cushing's syndrome primarily because of an atrophy of the paraventricular and supraoptic nuclei or because of depression by a raised intraventricular pressure, a decrease in the secretion of the neural hypophysis results in a hyalinization of the basophile cells and a preponderance with overaction of the eosinophile cells. Among the effects invariably produced are diastolic hypertension and arteriosclerosis. These effects are considered to result from a narrowing of the extrarenal blood vessels and of the efferent glomerular arterioles. Because of the latter action, renin is released. It is the combined action of these hormones in persons whose neural hypophysis is depressed and whose blood vessels are, therefore, sensitized to the constrictive action of these hormones that hypertension is attributed. There appears also to be a constitutional susceptibility in addition.

Overaction of the eosinophile cell-adrenal cortical hormone complex results in an increased formation and storage of neutral fat and of cholesterol. This is considered of primary significance in the development of arteriosclerosis.

Hypertension is regarded as the reaction of the body to any inadequacy of renal tubular function. It is part of the mechanism for compensating with increased blood flow the deficiency of the renal tubular mass. Renin is regarded as the substance released by the kidney tubules which not only constricts vessels outside the kidney directly, but also stimulates the eosinophile cells of the glandular hypophysis and thereby increases the cardiac output and renal tubular function. In combination with the desoxycorticosterone fraction of the adrenal cortical hormone it leads to extrarenal vascular constriction, but without constricting the blood vessels to the renal tubules themselves.

In persons with essential hypertension, the depression of the neural hypophysis is regarded as, first, functional because of nervous influences, particularly from the frontal lobes; later, particularly in the malignant phase, it is regarded as organic as well, because of the increased intraventricular pressure acting on the cells of the supraoptic and the paraventricular nuclei.

Constitutional susceptibility, both of the nervous system to the depression of the hypothalamic nuclei and of the blood vessels to the constricting action of the hormones responsible for the extrarenal vasoconstriction, is postulated for persons with essential hypertension.

In persons with essential hypertension, the depression of the basophile cells and the stimulation of the eosinophiles presumably are functional, as obvious structural alterations have not been demonstrated.

In pregnancy, the eosinophile cell preponderance is regarded as the result of the inactivation of the secretion of the neural hypophysis by progesterone. The eosinophile overaction here, as elsewhere, stimulates the adrenal glands and in those individuals who are emotionally and constitutionally susceptible it would be expected to result in sufficient constriction of the efferent glomerular arterioles to release renin. As in essential hypertension, the combined action

of these three hormones together with that of progesterone on vessels sensitized by depression of the neural hypophysis is regarded as primarily responsible for the initiation of diastolic hypertension.

Evidence to support the concept of the pathogenesis of essential hypertension herein presented is sought in the accepted importance of emotional influences in its development. The frequent association of obesity, of premature ageing, of decreased insulin sensitivity, and of increased intracranial pressure, particularly in later stages of essential hypertension, is considered to support the probability of the hypothesis presented. The fact that the characteristics of the circulation in essential hypertension are similar to those which exist in the hypertension associated with Cushing's syndrome where such a mechanism has been established is regarded as supporting its probability.

In essential hypertension the sympathetic nervous system and epinephrine are regarded as mechanisms for rapid homeostatic adjustments of the renal circulation, but they are not considered of primary importance in the pathogenesis of such hypertension.

The concept affords a mechanism for explaining the prevailing earlier and wider incidence of hypertension and arteriosclerosis in response to the stress and strain of modern existence.

REFERENCES

1. Heinbecker, Peter: Cushing's Syndrome, Ann. Surg. **124**: 252-261, 1946.
2. Heinbecker, Peter: Factors Limiting Surgery for Essential Hypertension, Ann. Surg. **126**: 535-544, 1947.
3. Heinbecker, P., White, H. L., and Rolf, D.: The Essential Lesion in Experimental Diabetes Insipidus, Endocrinology **40**: 104-113, 1947.
4. Rasmussen, A. T.: Effects of Hypophysectomy and Hypophysial Stalk Resection on Hypothalamic Nuclei of Animals and Man, A. Research Nerv. & Ment. Dis., Proc. **20**: 245-269, 1940.
5. Heinbecker, P., and White, H. L.: Hypothalamico-Hypophysial System and Its Relation to Water Balance in the Dog, Am. J. Physiol. **133**: 582-593, 1941.
6. Greving, R.: Makroskopische Anatomie und Histologie des vegetativen Nervensystems. Bumke und Foerster, Handbuch Neurologische, vol. 1, Berlin, 1935, Julius Springer, pp. 810-886.
7. Heinbecker, Peter: The Pathogenesis of Cushing's Syndrome, Medicine **23**: 225-247, 1944.
8. Heinbecker, Peter: Unpublished data.
9. Heinbecker, Peter: Unpublished data.
10. Victor, J.: Hypertension Produced in Dogs by Unilateral Ligation of Periadrenal Blood Vessels and Tissue, Proc. Soc. Exper. Biol. & Med. **60**: 332-334, 1945.
11. Heinbecker, Peter: 1944, loc. cit.
12. Heinbecker, Peter: Studies on the Sensitivity of Smooth Musculature to Exogenous Epinephrine, Am. J. Physiol. **118**: 276-284, 1937.
13. Goldblatt, H.: Experimental Hypertension Induced by Renal Ischemia, Harvey Lecture, Bull. New York Acad. Med. **14**: 523-553, 1938.
14. Kohlstadt, K. G., Helmer, O. M., and Page, I. H.: Activation of Renin by Blood Colloids, Proc. Soc. Exper. Biol. & Med. **39**: 214-215, 1938.
15. White, H. L., Heinbecker, P., and Rolf, D.: Some Endocrine Influences on Renal Function and Cardiac Output, Am. J. Physiol. **149**: 404-417, 1947.
16. White, H. L., Heinbecker, P., and Rolf, D.: 1947, loc. cit.
17. Heinbecker, P., White, H. L., and Rolf, D.: Effects of Hypophysectomy on Some Renal Functions, Proc. Soc. Exper. Biol. & Med. **45**: 44-47, 1941.
18. Ragan, C., Ferrabee, J. W., Phyfe, P., Atchley, D. W., and Loeb, R. F.: A Syndrome of Polydipsia and Polyuria Induced in Normal Animals by Desoxycorticosterone Acetate, Am. J. Physiol. **131**: 73-78, 1940.
19. Mulinos, M. G., Spingarn, C. L., and Lojkin, M. E.: Desoxycorticosterone and Diabetes Insipidus-like Condition, Am. J. Physiol. **135**: 102-112, 1941.
20. Pickering, G. W., and Prinzmetal, M.: Effect of Renin on Urine Formation, J. Physiol. **98**: 314-335, 1940.
21. Smith, H. W.: Studies in the Physiology of the Kidney, Lawrence, Kansas, 1939, Univ. of Kansas, Univ. Extension Division.

22. Corcoran, A. C., Kohlstadt, K. G., and Page, I. H.: Changes of Arterial Blood Pressure and Renal Hypodynamics by Injection of Angiotonin in Human Beings, Proc. Soc. Exper. Biol. & Med. **46**: 244-248, 1941.
23. Goldring, W., Chasis, H., Ranges, H. A., and Smith, H. W.: Effective Renal Blood Flow in Subjects With Essential Hypertension, J. Clin. Investigation **20**: 637-653, 1941.
24. Tigerstedt, R., and Bergman, P. G.: Niere und Kreislauf, Skandinav. Arch. f. Physiol. **8**: 223-271, 1898.
25. Goldblatt, H., Lynch, J., Hanzol, R. F., and Summerville, W. W.: Studies on Experimental Hypertension; Production of Persistent Elevation of Systolic Blood Pressure by Means of Renal Ischemia, J. Exper. Med. **59**: 347-379, 1934.
26. Braun-Menendez, E., Fasciolo, J. C., Leloir, L. F., Munoz, J. M., and Taquini, A. C.: Renal Hypertension, Springfield, Ill., 1946, Charles C Thomas, Publisher.
27. (a) Pickering, G. W.: The Circulatoin in Arterial Hypertension, Brit. M. J. **2**: 1-4, 31-34, 1943.
(b) Heinbecker, Peter: Unpublished data.
28. Gaunt, R., and Hays, H. W.: The Life-Maintaining Effects of Crystalline Progesterone in Adrenalectomized Ferrets, Science **88**: 576-577, 1938.
29. McKeown, T., and Spurrell, W. R.: The Results of Adrenalectomy in the Pregnant Albino Rat, J. Physiol. **98**: 255-262, 1940.
30. Thorn, G. W., and Engel, L. L.: The Effect of Sex Hormones on the Renal Excretion of Electrolytes, J. Exper. Med. **68**: 299-312, 1938.
31. Reynolds, S. R. M., and Allen, W. M.: Physiology of the Corpus Luteum, Am. J. Obst. & Gynec. **30**: 309-318, 1935.
32. Knaus, H.: Experimentelle Untersuchungen zur Physiologie und Pharmakologie der Uterusmuskulatur in der Schwangerschaft, Arch. f. exper. Path. u. Pharmakol. **124**: 152-184, 1927.
33. Norris, E. H.: Arrhenoblastoma, Am. J. Cancer **32**: 1-29, 1938.
34. Zondek, B.: Clinical and Experimental Investigations on the Genital Functions and Their Hormonal Regulation, Baltimore, 1941, Williams & Wilkins Company.
35. Heinbecker, P.: 1944, loc. cit.
36. Heinbecker, P. : 1946, loc. cit.
37. Crooke, A. C.: Change in Basophil Cells of Pituitary Gland Common to Conditions Which Exhibit Syndrome Attributed to Basophil Adenoma, J. Path. & Bact. **41**: 339-349, 1935.
38. Heinbecker, P., White, H. L., and Rolf, D.: Experimental Obesity in the Dog, Am. J. Physiol. **141**: 549-565, 1944.
39. Pickering, G. W.: The Peripheral Resistance in Persistent Arterial Hypertension, Clin. Sc. **2**: 209-235, 1935.
40. Goldring, W., Chasis, H., Ranges, H. A., and Smith, H. W.: 1941, loc. cit.
41. Goldblatt, H., Lynch, J., and Hanzol, R. F.: 1934, loc. cit.
42. Braun-Menendez, E., and others, 1946, loc. cit.
43. Corcoran, A. C., and Page, I. H.: Renal Aspects of Experimental and Clinical Hypertension, J. Lab. & Clin. Med. **26**: 1713, 1941.
44. Weiss, Edward (Philadelphia): Psychosomatic Aspects of Hypertension, J. A. M. A. **120**: 1081-1086, 1942.
45. Binger, C. A. L., Ackerman, N. W., Cohn, A. E., Schroeder, H. A., and Steele, J. M.: Personality in Arterial Hypertension. Psychosomatic Medicine Monographs, New York, 1945, Am. Soc. for Research in Psychosom. Probl., Inc.
46. Smith, H. W.: The Physiology of the Kidney, London, 1937, Oxford University Press.
47. Friedman, M., and Kaplan, A.: Studies Concerning the Site of Renin Formation in the Kidney, J. Exper. Med. **77**: 65-70, 1943.
48. Farris, Edmond J., Yeakel, E. H., and Medoff, H. S.: Development of Hypertension in Emotional Gray Norway Rats After Air Blasting, Am. J. Physiol. **144**: 331-333, 1945.
49. Goldblatt, H.: The Renal Origin of Hypertension, Physiol. Rev. **27**: 120-165, 1947.
50. Heinbecker, P.: 1946, loc. cit.
51. (a) Rasmussen, A. T.: 1940, loc. cit.
(b) Rasmussen, A. T.: The Relation of the Basophilic Cells of the Human Hypophysis to Blood Pressure, Endocrinology **20**: 673-678, 1936.
52. Terry, A. H., Jr.: Obesity and Hypertension, J. A. M. A. **81**: 1283-1284, 1923.
53. Westphal, K.: Pathogenesis of Essential Arterial Hypertension; Paradoxical Vascular Reaction Following Compression in Arterial Hypertension, Ztschr. f. klin. Med. **101**: 545-557, 1925.
54. Joslin, Elliott P., and others: Treatment of Diabetes Mellitus, ed. 3, Philadelphia, 1923, Lea & Febiger, p. 578.
55. Alvarez, W. C., and Zimmermann, A.: Blood Pressure in Women as Influenced by Sexual Organs, Arch. Int. Med. **37**: 597-636, 1926.
56. Heinbecker, P.: 1946, loc. cit.
57. Heinbecker, P.: 1944, loc. cit.

INDICATIONS FOR SYMPATHECTOMY IN THE TREATMENT OF HYPERTENSION

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ANY internist who has the privilege of studying a large number of patients with hypertension before and after sympathectomy must be impressed by certain facts—that the operation has not yet been placed on a rational basis; that it seldom, if ever, produces manometric cure; that it is often followed by spectacular amelioration of symptoms; that the results are apt to be temporary; and finally that this treatment is violent. Until these points are properly appreciated and the limitations of sympathectomy thus recognized, the indications for surgical intervention will remain confused in the minds of many.

Since the cause of essential hypertension is unknown, all therapy is empirical. The one known basic fact is that elevation of blood pressure is due to increased peripheral resistance, but there is as yet no agreement as to whether the arteriolar constriction is of humoral or nervous origin. If the surgeon believes the former explanation to be true, he must show that sympathectomy modifies the endocrine system in an appropriate manner; if he accepts the latter view, he justifies the operation more easily in his own mind.

There are, of course, many factors in the normal organism which play upon smooth muscle in such a way as to increase its tonus. Fig. 1 is a naive representation of the fact that clinical hypertension does not occur until the sum of these vasoconstrictor influences exceeds a certain but unknown threshold. The illustrated sizes of the various fragments, however, are in no way to be interpretated as a quantitative expression of their relative importance, for our present knowledge is much too meager to permit any such assumption; it is obvious also that each patient will present his own individual pattern. If it is recalled that hypertension is not a disease but a symptom, it is worth while to speculate concerning the manner in which sympathectomy can be expected to modify or abolish each of these vasoconstrictor forces.

Surgical measures are certainly incapable of modifying the genetic influences which make one person's blood vessels more responsive than another's to a given set of stimuli. Primary vascular disease is represented because there is as yet no definite assurance that at least some cases of clinical hypertension may not be initiated by obliterative arterial disease in strategic locations; whatever the sequence may be, sympathectomy is surely an unsatisfactory remedy for arteriosclerosis. One surgeon[24] justifies sympathectomy on the grounds that it improves renal blood flow despite the facts that the renal circulation is autonomously regulated in normal man,[28] that renal ischemia is inconstantly present

Read at the thirty-third annual session of the American College of Surgeons, Sept. 11, 1947, New York, N. Y.

in hypertension,[23] and that sympathectomy does not increase the renal clearances of certain test materials.[3, 9, 10, 31]

The relationship between renal disease and sympathectomy cannot be lightly dismissed, however, since there is now reason to believe that chronic overproduction of the renal enzyme (renin) may lead to a persistent nonrenal (neurogenic ?) type of hypertension.[21] These experimental findings are in harmony with the clinical experience that nephrectomy is usually not successful in relieving long-standing hypertension associated with unilateral renal disease[2] and that sympathectomy is often surprisingly helpful in cases of chronic bilateral renal disease.[1, 5, 19, 29] The inference has been made that even in "renal" hypertension, the nervous system is sufficiently disturbed to justify sympathectomy. This operation is said by some to be helpful because it decreases peripheral resistance by paralyzing a large portion of the vascular bed. However, the evidence offered in support of this contention needs critical examination.

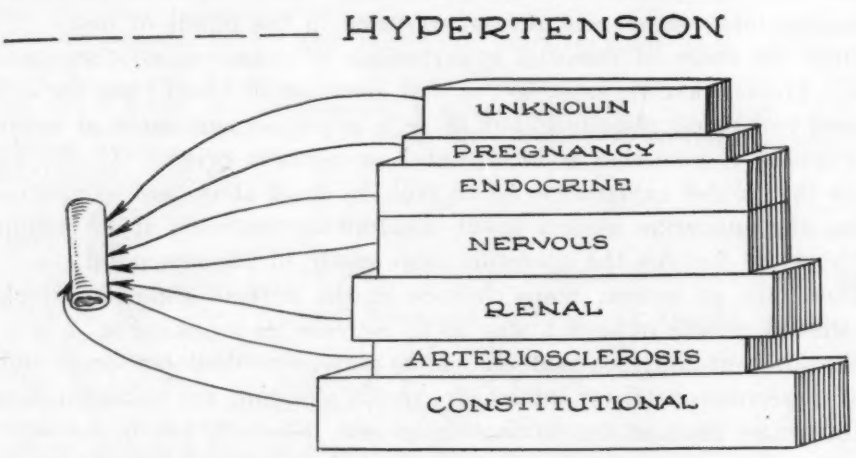

Fig. 1.—Hypertension is the summation of many vasoconstrictor forces.

The existence of neurogenic clinical hypertension has often been postulated[6, 11, 18, 22] but the data can be interpreted in other ways. It may be that as some persons grow older and their cerebral neurons atrophy, the blood pressure may rise because of lack of cerebral inhibition,[7] but such individuals are commonly thought to be unsuitable for operation because of age and arteriosclerosis. There appears to be no good evidence, however, that presenile essential hypertension is ever due to overactivity of the sympathetic nervous system and there is much persuasive evidence that it is not.[25, 26, 30]

Any enlargement of the vascular bed which follows sympathectomy is probably temporary because of the capacity of the peripheral vasomotor apparatus to regain its former tone and size. In our experience with about 100 hypertensive patients who have been subjected to bilateral splanchnicectomy and excision of both sympathetic chains from the fourth or fifth thoracic through the second lumbar ganglia we[20] have yet to see anything resembling a "cure" and have invariably found that the blood pressure slowly rises postoperatively

to or somewhat below the preoperative level. This recrudescence of hypertension is not due to an increase in blood volume[4] and we believe it is due to the autonomous action of peripheral arterioles. Postural hypotension is the only phenomenon which we can clearly attribute to vascular denervation and, as shown in Fig. 2, this disappeared within one year in the vast majority of our cases. We, therefore, look upon postural hypotension as an undesirable surgical complication rather than an asset and believe that such reduction in blood pressure as may persist after sympathectomy is due to vascular relaxation from causes other than denervation of the splanchnic bed and legs. Denervation of the splanchnic bed may, it is true, abolish certain visceral reflexes in a helpful manner and extensive sympathectomy may to a certain extent protect peripheral vessels from fluctuation in vasomotor tone, but these effects are of themselves too minor to justify radical surgical procedures. It is difficult to accept radical sympathectomy as a form of treatment for what appears to be a humoral disease.

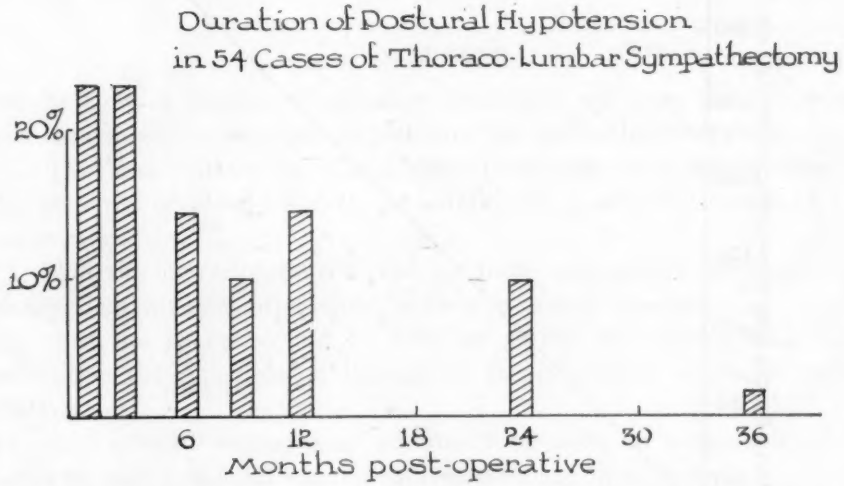

Fig. 2.—Postural hypotension is a temporary postsympathectomy response.

Since the weight of present evidence is in favor of a humoral origin of hypertension, the possibility should be considered that sympathectomy is able to modify the chemical composition of the blood in some favorable manner. Heinbecker's[12-15] highly original observations led him to conclude that hypofunction of the neurohypophysis sensitizes blood vessels to a variety of pressor substances such as renin, epinephrine, and progesterone. If confirmed by others, this view is of great theoretical and practical importance because it offers an explanation of the pathogenesis of hypertension and suggests that sympathectomy induces vascular relaxation by diminishing the activity of the adrenal medulla. From the surgical standpoint this theory is perhaps compromised by evidence that epinephrine output is not abolished by adrenal denervation,[16] but even diminished secretion should be helpful since epinephrine is a substance with definite analeptic and vasoconstrictor properties. It may also regulate the activity of the adrenal cortex,[17] a gland currently suspected of playing an important role in the etiology of hypertension.

Further speculation at this time would be unprofitable but our experience with the surgical treatment of hypertension is such as to incline us toward the view that sympathectomy relieves symptoms and occasionally lowers blood pressure through some humoral mechanism rather than by denervation of peripheral arterioles. If this be true, then the operation should be regarded as palliative rather than curative and extensive sympathectomy would be unphysiologic. In common with other observers we have noted a high incidence of symptomatic relief after sympathectomy and we agree that there is no correlation between the degree of subjective improvement and the postoperative blood pressure levels. This has led some to conclude that the clinical improvement is due entirely to suggestion. This point of view may be correct but it implies, first, that nearly

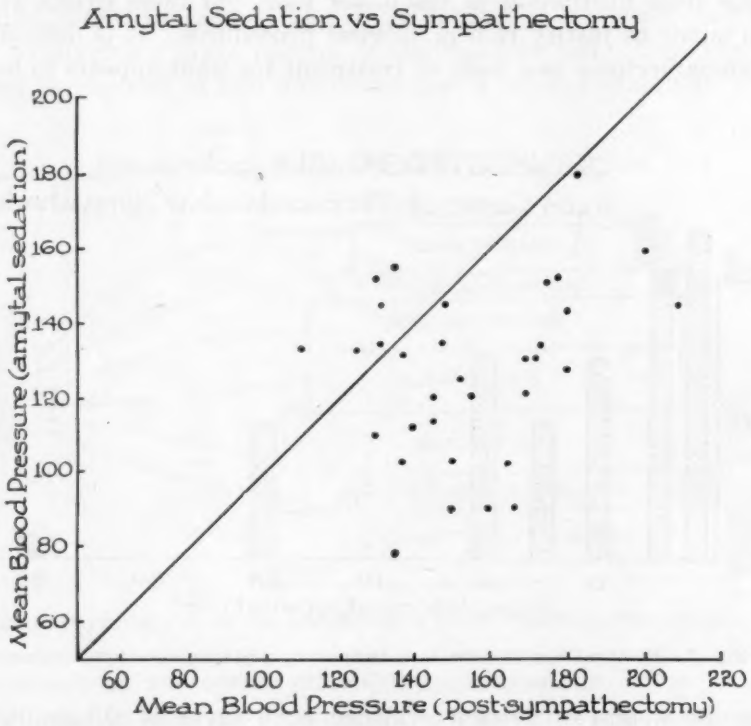

Fig. 3.—Lack of correlation between the sodium amytal sedation test and the postoperative results.

every patient with symptomatic hypertension is psychoneurotic and, second, that this is a special kind of psychoneurosis in that it responds instantly and with more or less permanence to one treatment. Most psychoneuroses, of course, yield only, if at all, to firm and continued pressure. It is difficult to persuade anyone in close contact with a large number of sympathectomized hypertensive patients that the surgeon has performed only a psychotherapeutic act. In our experience it has been rare to find a patient who is not glad he has had the operation and we have seen no comparable results accomplished by standard psychiatric methods. We are convinced that sympathectomy performs some useful physiologic function in some patients. At the moment it appears possible that adrenal denervation is the essential feature but the additional effect of cardiac denervation is worthy of study.

Patients should, therefore, not be selected for operation solely on the basis of tests which measure only blood pressure fluctuations. Certainly such procedures as the cold pressor test, the amytal sedation test, splanchnic block, and the induction of high spinal anesthesia have proved notoriously unreliable as gauges of postsympathectomy results. Fig. 3 illustrates our experience with the sodium amytal test; little correlation is seen between the lowest mean blood pressure reading obtained by heavy sedation and the mean pressure six to twelve months after thoracolumbar sympathectomy. Usually the amytal test gave falsely optimistic results, although the few cases above the line ran in the opposite direction. We have had no experience with high caudal anesthesia as recommended by Russek, Southworth, and Zohman[27] but doubt, on theoretical grounds, that it will prove to be more accurate. Disappointments will be fewer if the operation is reserved for those with disabling symptoms and early malignant hypertension, but the manometric results will, of course, be better if the patient also has a labile blood pressure. It also seems reasonable to try a low sodium regimen first,[8] but we have had little success with it thus far.

CONCLUSIONS

At the time of this communication, therefore, we make the following suggestions regarding the selection of patients for sympathectomy:

(1) That less reliance be placed upon prediction tests which measure the response of blood pressure to sedation or to anesthetization of the nervous system,

(2) that the operation be reserved for those with severe symptoms but no gross impairment of cerebral, cardiac, or renal function,

(3) that the operation not be done on young individuals with mild asymptomatic hypertension because of the possibility of nerve regeneration,

(4) that sympathectomy may profitably be done on patients over 50 years of age, provided other requirements are met, and

(5) that patients be told that sympathectomy offers palliation and not cure.

REFERENCES

1. Ayman, D., and Goldshine, A. D.: New England J. Med. **229**: 797, 1943.
2. Barker, N. W., and Braasch, W. F.: Internat. Abstr. Surg., 1947; Surg., Gynec. & Obst. **84**: 299, 1947.
3. Corcoran, A. C., and Page, I. H.: Arch. Surg. **42**: 1072, 1941.
4. Davis, W. D., Jr., and Mayerson, H. S.: Unpublished data.
5. de Takats, G., and Fowler, E. F.: SURGERY **21**: 773, 1947.
6. Dock, W.: Am. J. Physiol. **130**: 1, 1940.
7. Dock, W.: New York State J. Med. **45**: 93, 1945.
8. Dock, W.: Rocky Mountain M. J. **44**: 372, 1947.
9. Findley, T., Clinton, E., and Edwards, J. C.: SURGERY **12**: 64, 1942.
10. Goldring, W., and Chasis, H.: Hypertension and Hypertensive Disease, London, 1944, Commonwealth Fund, p. 157.
11. Gregory, R., Levine, H., and Lindley, E. L.: Texas Rep. Biol. & Med. **2**: 121, 1944.
12. Heinbecker, P.: Medicine **23**: 225, 1944.
13. Heinbecker, P.: Ann. Surg. **124**: 252, 1946.
14. Heinbecker, P.: Ann. Surg. **126**: 535, 1947.
15. Heinbecker, P.: SURGERY **23**: 618, 1948.
16. Kobro, M.: Acta med. Scandinav. **126**: 97, 1946.

17. Long, C. N. H., and Fry, E. G.: Proc. Soc. Exper. Biol. & Med. **59**: 67, 1945.
18. Medoff, H. S.: Am. J. Physiol. **143**: 300, 1945.
19. Nesbit, R. M., and Plumb, R. T.: J. Urol. **57**: 116, 1947.
20. Ochsner, A., and Findley, T.: Unpublished data.
21. Miner, R. W.: Experimental Hypertension, New York, 1946, New York Academy of Sciences, p. 153.
22. Page, I. H.: New York State J. Med. **44**: 2686, 1944.
23. Page, I. H., and Corcoran, A. C.: Arterial Hypertension, Chicago, 1945, The Year Book Publishers, Inc., p. 249.
24. Peet, M. M.: New England J. Med. **236**: 270, 1947.
25. Pickering, G. W.: Clin. Sc. **2**: 209, 1936.
26. Prinzmetal, M., and Wilson, R.: J. Clin. Investigation **15**: 63, 1936.
27. Russek, H. I., Southworth, J. L., and Zohman, B. L.: J. A. M. A. **130**: 927, 1946.
28. Smith, H. W.: J. Clin. Investigation **18**: 319, 1939.
29. Smithwick, R. H.: Arch. Surg. **49**: 180, 1944.
30. Stead, E. A., Jr., and Kunkel, P.: J. Clin. Investigation **19**: 25, 1940.
31. Talbott, J. H., and others: J. Clin. Investigation **22**: 387, 1943.

GUNSHOT WOUNDS INVOLVING THE ABDOMINAL AORTA

A Report of Two Cases

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PENETRATING wounds involving the aorta which permit the victim to survive for a sufficient time for surgical care are exceedingly few, and instances of successful treatment of such wounds have been reported rarely. Dshanelidze,[1] Blalock,[2] and Elkin[3] have each reported successful suture of a stab wound of the ascending portion of the thoracic aorta. The latter two authors reported wounds which had been caused by ice picks and were only tiny perforations. Wildegans[4] in 1926 reported a case in which a 1 cm. stab wound of the abdominal aorta was successfully repaired. Dubinskiy[5] in 1944 sutured a 0.3 cm. shrapnel wound of the abdominal aorta followed by recovery of the patient. In a comprehensive review of the literature no instance of the survival of a patient after the repair of a direct bullet injury of the abdominal aorta has been found.

It has been my unique experience to encounter and treat successfully in a period of eight months two patients with gunshot wounds of the abdominal aorta. In the first instance a vitallium tube was utilized to maintain the continuity of the vessel, while in the second direct suture was possible. The first case is believed to be the only one in which a vitallium tube has been placed in the human aorta with a successful result.

CASE REPORTS

Case 1 (No. 209392).—C. J., a 26-year-old Negro woman, was brought to the hospital at 7:40 P.M. on Dec. 28, 1945, forty minutes after having been shot in the abdomen with a 32 caliber revolver. She was in severe shock, pulseless, with a blood pressure too low to record, but was conscious and complaining of abdominal pain. She was moderately obese but normal except for the findings related to the injury. Respiratory rate was 30 and cardiac rate 100 per minute. Over the left rectus muscle, midway between the umbilicus and the xiphoid process, was a bullet wound .5 cm. in diameter. There was no wound of exit. The abdominal wall was splinted and diffusely tender. Peristaltic sounds were absent and a fluid wave was demonstrable. Rectal examination was unremarkable. A neurologic examination was not performed but it was noted that the patient was able to move all extremities.

A Levine tube was passed into the stomach and a small amount of fresh blood was aspirated. Urinalysis was negative for blood. After the intravenous administration of 1000 c.c. of plasma the blood pressure rose to 100/70 and the condition was greatly improved. Roentgenologic survey of the body showed a bullet adjacent to the neck of the left femur (Fig. 1).

Under endotracheal cyclopropane and ether anesthesia a long left rectus incision was made, with a transverse extension to the right. Approximately 500 c.c. of fresh blood were evacuated from the peritoneal cavity, but no persistent bleeding was observed. Exploration of the abdominal viscera revealed that the bullet had passed through the anterior wall of

Received for publication, June 23, 1947.

the stomach near the pylorus, through the posteroinferior wall of the first portion of the duodenum, and through the head of the pancreas into the retroperitoneal area. There was a large retroperitoneal hematoma around the head of the pancreas and at the base of the transverse mesocolon. The gastric and duodenal perforations were closed with silk mattress sutures.

In order to explore the retroperitoneal hematoma the operator divided the lateral peritoneal attachments of the second and third portions of the duodenum and the hepatic flexure of the colon and retracted these structures toward the midline. As the hematoma was being cleared away, there was a tremendous spurt of blood from the depths of the operative area. Digital pressure was applied immediately to check the hemorrhage. Palpation revealed that the blood was coming from a wound in the aorta. With the hemorrhage controlled by

Fig. 1.—Roentgenogram three months after injury showing bullet in relation to neck of left femur and tube in aorta overlying the third lumbar vertebra.

digital pressure on the wound, the aorta was mobilized and strips of cotton tape were passed around it and twisted down. The field was then cleared of blood revealing a perforation through the aorta 5 mm. in diameter extending in an anteroposterior direction (Fig. 2). By palpation it was established that the wound lay 6 cm. above the aortic bifurcation, presumably below the origin of the inferior mesenteric artery. The edges of the wounds were ragged and there was considerable loss of substance in the damaged segment. An unsuccessful attempt was made to close the perforations with silk sutures. Ligation of the vessel was deemed inadvisable because of the possibility of secondary hemorrhage or gangrene of the lower extremities. It was therefore decided to attempt re-establishment of the continuity of the aorta by means of a vitallium tube. Although the largest tube available was only 5 mm. in diameter, it was felt that a lumen of this size would permit adequate blood flow to the lower extremities until collateral flow could be established. The

anterior bullet wound was enlarged slightly and the tube slipped into the lumen of the aorta. A silk ligature had been attached to the tab in the middle of the tube in order to control it. A heavy braided silk ligature was then tied around the aorta and the tube on either side of the damaged area. Because of the possibility that these ties might cut through, a strip of ¼ inch cotton tape was tied down flatly on each side of the pair of silk ligatures (Fig. 3). When the tourniquets were released, no leakage occurred, and palpation revealed fairly strong pulsations in the common iliac arteries. No further injuries were found upon completion of abdominal exploration. Cigarette drains were placed in the retroperitoneal tissues in both lumbar areas and brought out through a stab wound in each flank. The abdominal incision was closed using through-and-through steel wire stay sutures. The skin was closed with fine cotton sutures.

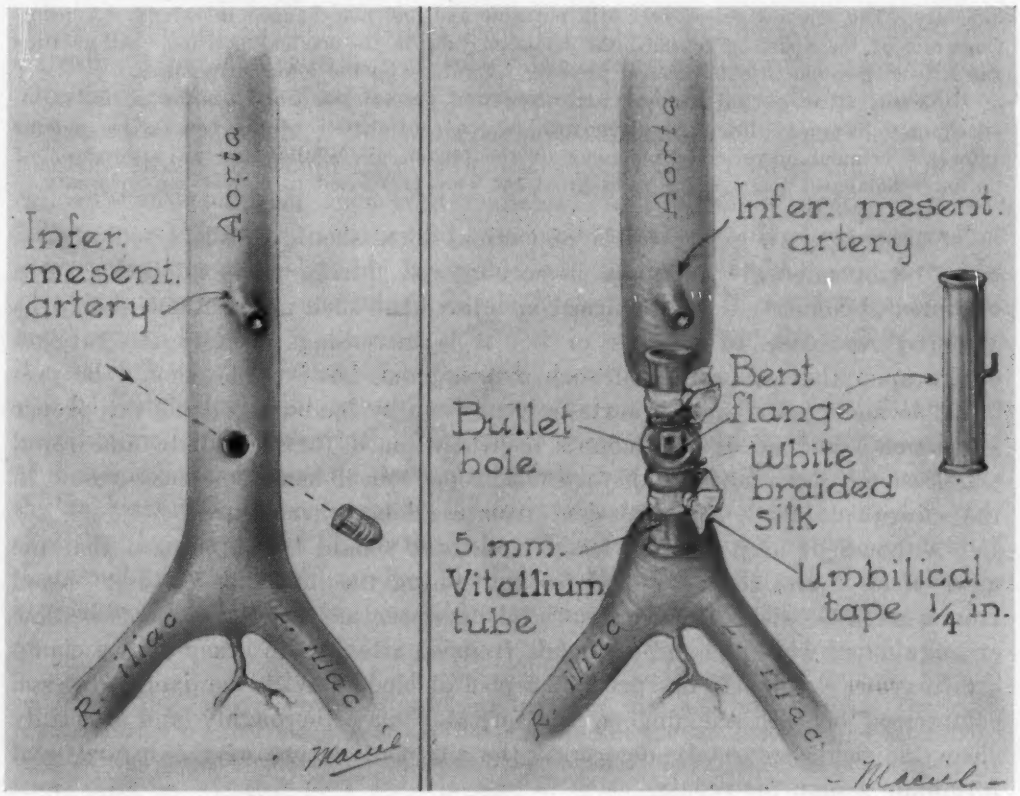

Fig. 2.—Diagram showing the course of the bullet and the location of the wound.
F.g. 3.—Drawing showing method of fixation of the tube within the lumen of the aorta.

During the procedure the patient's blood pressure never fell below 90/50, 1000 c.c. of plasma and 2500 c.c. of whole blood having been given.

The postoperative course was uncomplicated except for a transfusion reaction on the sixth day. Continuous gastric suction was maintained for two and one-half days, following which the Levine tube was removed and progressive feedings started. Sulfadiazine was given for eight days and penicillin for twenty-five days. The incision healed per primam.

In an attempt to prevent thrombosis at the site of repair and in the lower extremities, administration of dicoumarin was begun on the third day. A total of 650 mg. was given in the next twelve days, maintaining the prothrombin time between 30 and 38 seconds, the normal control being 15 seconds.

On the first day after operation it was noticed that the right calf was tender and enlarged. There was a complete foot drop on the right and 50 per cent reduction in the power of plantar flexion of the ankle. There was anesthesia over the entire foot in the distribution of the fifth lumbar and first sacral nerve roots. Both feet were warm and both femoral pulses were palpable though diminished in volume. The weakness and anesthesia were interpreted as evidence of direct injury to the nerve roots. During the forty-one days of her stay in the hospital there was gradual improvement of muscle power and diminution of the area of anesthesia. The femoral pulses did not change and on several occasions faint pulsations in both dorsalis pedis arteries were felt. Oscillometric readings on the lower extremities indicated that the pulsations were diminished about 75 per cent.

Following discharge from the hospital she gradually regained strength and returned to her household duties. Examination seventeen months after operation revealed no change in blood pressure or in the size of the heart. She could walk briskly a hundred yards without difficulty. The femoral pulses were still palpable and had not changed in volume. A roentgenogram of the abdomen revealed the vitallium tube in its original position. At no time has it been possible to obtain blood pressure recordings on the lower extremities.

As a result of partial paralysis and atrophy of the anterior tibial muscles on the right, an equinus deformity developed along with flexion contractures of the toes. Nine months after the original operation a tenotomy of the tendon of Achilles and an arthrodesis of the interphalangeal joint of the right great toe were performed to correct the deformity.

Comment.—An injury to the abdominal aorta should be suspected when a large retroperitoneal hematoma is encountered during the exploration of a wounded abdomen. It is our firm conviction that such a hematoma should be explored regardless of whether or not it is increasing. Before the surgeon enters upon the exploration of such a hematoma, however, he should be prepared to manage a damaged aorta or vena cava by having available the proper instruments and adequate amounts of whole blood for immediate and rapid transfusion. Reluctance to disturb a retroperitoneal hematoma may result in the subsequent death of the patient from secondary hemorrhage.

Although it may seem perfectly obvious it should be emphasized that the most effective and safest method for controlling the immediate gush of blood from a large vessel is digital pressure. I have seen at least two patients become exsanguinated while the surgeon made frenzied attempts to grasp with a clamp a torn vessel completely obscured by a pool of blood. With the damaged vessel compressed beneath the fingers, the operator may thoroughly and carefully clean the field, accurately determine the site and nature of the injury, and formulate a plan for repair.

The method of management must of course vary according to the nature of the wound. In the previously reported successful cases and in my second case simple suture was the method of choice. This is certainly the ideal mode of management of such a wound because it restores continuity of the vessel with a minimum of trauma and decreases the danger of intravascular thrombosis. In the case described, however, because of loss of substance and extensive damage to the wall of the vessel, simple suture of the perforations was not possible. Three methods of management were considerd. Ligation was rejected because of the danger of gangrene of the lower extremities or hemorrhage due to cutting through of the ligatures. Elkin[6] in 1940 collected twenty-four cases of ligation of the abdominal aorta and added one of his own. In only ten of these cases

was ligation complete and only seven of the patients survived the operation. No case of successful ligation of the aorta for traumatic injury has been found in the literature.

The second possible method, and the ideal one in this case, resection of the damaged segment with end-to-end anastomosis, would perhaps have been feasible in the hands of a surgeon experienced in the technique and under ideal conditions. However, because of the precarious condition of the patient and because of the operator's lack of experience in the anastomosis of blood vessels this procedure was deemed too hazardous and time consuming to be attempted.

The third method, repair of the vessel by means of a vitallium tube, seemed to offer the best hope of success and certainly was the most simple in the case reported. Tuffier[7] in 1915 described a method of blood vessel anastomosis using a paraffin-coated silver tube. Blakemore and Lord[8] have devised a nonsuture method of blood vessel anastomosis employing vitallium tubes lined with a segment of vein. This work suggested the mode of management of the case described. It would have been desirable to have used a tube of larger caliber than 5 mm. had such been available. At the time of operation it was fully expected that the tube would sooner or later be occluded by a thrombus inasmuch as no intimal lining was provided. This has not, however, been the case as far as can be determined. It is likely that the increase in velocity of flow through the tube due to the diminution in the lumen of the vessel accounts for the lack of coagulation.

Although desirable, determinations of the pressure in the femoral arteries were not made because of lack of the appropriate apparatus and because of fear of damaging the vessels and producing thrombosis. There is, however, convincing evidence that the pressure in the arterial system distal to the tube is considerably less than that above the tube. The femoral pulse volume is greatly decreased and the dorsalis pedis pulses are only occasionally palpable. Oscillometric readings show pulsations which are much smaller than normal.

CASE 2 (No. 45171).—W. B., a 28-year-old white man, was brought to the hospital on Aug. 8, 1946, thirty minutes after having been shot with a 22 caliber rifle. The bullet passed through the soft tissue medial to the distal end of the left humerus and entered the chest through the left tenth rib interspace in the posterior axillary line. He was in moderately severe shock as evidenced by a blood pressure of 80/40 and a cold, clammy, ashen skin. Physical examination of the chest corroborated by roentgenograms, revealed no signs of pneumothorax, hemothorax, or pulmonary trauma. The abdomen was full, doughy, diffusely tender, and moderately rigid. The urine was grossly bloody. Roentgenograms showed the bullet in the pelvis.

Blood and plasma transfusion was started through a cannula in the right saphenous vein and the patient was prepared for operation. Despite rapid administration of 1500 c.c. of plasma and whole blood his condition failed to improve and the blood pressure began to fall. Increasing distention of the abdomen indicated rapid intraperitoneal hemorrhage. Therefore, under drop ether anesthesia the abdomen was opened by means of a long left rectus incision. A large amount of blood was encountered in the peritoneal cavity. After evacuation of most of the blood the origin of the hemorrhage was discovered to be in the gastrohepatic omentum where the main trunk of the left gastric artery had been severed. The distal cut end of the vessel was spurting vigorously. This was clamped and ligated with medium silk.

Exploration of the abdomen then revealed the bullet lying free in the cul-de-sac of Douglas. There was no injury to any portion of the gastrointestinal tract. A large retroperitoneal hematoma was discovered behind the splenic flexure of the colon. In order to expose the hematoma the parietal attachments of the splenic flexure were divided and the colon was mobilized medially by blunt dissection. The fascia of Gerota, distended with blood, was incised and the kidney palpated. Its entire upper one-third was shot away and there was active bleeding from the cut surface. Nephrectomy was done, the renal vessels and ureter being divided and ligated with double ligatures of braided silk.

Although this procedure served to control all bleeding the operator proceeded to explore the wound in the gastrohepatic ligament for the other end of the left gastric artery. During the search for the proximal end of the vessel there was a spurt of blood from deep in the retroperitoneal area. Digital pressure was applied and the area carefully exposed. A 1 cm. longitudinal rent was found in the anterior wall of the abdominal aorta. No other bleeding point could be found. It was postulated that the left gastric artery had in this case a separate origin from the aorta and that the bullet had passed through the junction of the artery with the aorta. The margins of the rent were grasped and approximated by means of Babcock intestinal forceps, while the wound was closed with a continuous locked suture of 00000 silk and several interrupted sutures of the same material. No leakage occurred from the aorta after release of the clamp.

The left kidney bed was drained by means of four lengths of Penrose tubing brought out through a stab wound in the left flank. The abdominal incision was closed with buried vertical figure-of-eight mattress sutures of No. 34 steel wire, and the skin was closed with fine silk.

At the end of the procedure the patient's blood pressure was 120/80 and his condition greatly improved. He received 2500 c.c. of whole blood and 750 c.c. of plasma during the operation, which lasted two hours and twenty minutes.

Postoperatively he was treated with penicillin, Wangensteen suction, and parenteral fluids. There was a marked oliguria and hemoglobinuria for two days, during which time the blood nonprotein nitrogen rose to 132 mg. per cent and periorbital edema appeared. This was attributed to a hemolytic transfusion reaction at the time of operation, and 0.6 molar sodium lactate was given, bringing the urinary pH from 5 to 7. By the fourth day the output was adequate and the azotemia subsided. Subsequent course was uneventful; the wound healed per primam, and he was discharged on the eighteenth day.

When seen nine months after the operation he was well and showed no sign of circulatory disturbance in the lower extremities. Blood pressure was 130/90. There was no mass or bruit over the upper abdomen.

Comment.—This case presented a much less difficult and complicated problem than did the first. The wound was tangential and consisted only of a small slit which was easily repaired. The importance of exploration of retroperitoneal hematomas is again illustrated. Failure to discover and repair injuries to retroperitoneal structures accounts for a large proportion of the preventable mortality in traumatic abdominal injuries.

DISCUSSION

Wounds of the aorta are found to be not necessarily fatal. Numerous cases have been reported in which persons have survived for varying periods of time up to ten years following aortic injuries.[9-30]

The survival of these patients has been attributed to three factors:

1. That the wound was small and became sealed by blood clot during the period of primary hemorrhagic shock.

2. That the injured portion of the aorta was in such a position that the surrounding tissues, together with the escaping blood, served as a tamponade.
3. That an acute arteriovenous fistula was formed allowing the return to the systemic circulation of much of the blood lost from the aorta.

The survival of both of the patients in my cases until the time of operation, which in each case was at least two hours after the injury, can be attributed to sealing of the wounds by blood clot and tamponade by blood extravasated into the retroperitoneal tissues.

Despite the fact that some patients survive injuries of the aorta, it should again be emphasized that failure to explore retroperitoneal hematomas is hazardous and may result in fatality from missed injuries to retroperitoneal viscera. It is also to be emphasized that anatomic reconstruction of an injured vessel is the desirable goal. This was accomplished in one of our cases while in the other, because of the circumstances, restoration of continuity with a vitallium tube was elected and proved successful.

SUMMARY

1. Two cases are reported in which a bullet wound of the abdominal aorta has been successfully repaired.

2. A review of the literature discloses only five previous instances of the successful repair of an aortic perforation.

3. Direct suture is the method of choice for repair of the aorta.

4. In one of my cases a nonsuture method utilizing a vitallium tube met with success when suture was not feasible.

5. The importance of exploration of retroperitoneal hematomas is emphasized.

REFERENCES

1. Dshanelidze, I. I.: Cited by Blalock.[2]
2. Blalock, A.: Successful Suture of a Wound of the Ascending Aorta, J.A.M.A. **103**: 1617-1618, 1934.
3. Elkin, D. C.: The Diagnosis and Treatment of Cardiac Trauma, Ann. Surg. **114**: 169-185, 1941.
4. Wildegans, Hans: Verletzungen der Aorta, Deutsche med. Wchnschr. **52**: 1810-1812, 1926.
5. Dubinskiy, M. D.: Sluckai shva bryushnoi aorti, Khirurgiya **4**: 71, 1944.
6. Elkin, D. C.: Aneurysm of the Abdominal Aorta, Ann. Surg. **112**: 895, 1940.
7. Tuffier: Intubation arteriélle substitutée à certaines ligatures immédiates des gros vaisseaux blessés, Presse méd. **23**: 416, 1915.
8. Blakemore, A. H., and Lord, J. W.: A Nonsuture Method of Blood Vessel Anastomosis, Ann. Surg. **121**: 435, 1945.
9. Heil: Beobachtung einer Verwundung der Art. Aorta ascendens, welche durch die Natur geheilt worden ist, Ztschr. f. d. Staatsarzneik. **33**: 458-460, 1837.
10. Bindemann: Eine Schussverletzung der Aorta abdominalis, Berl. klin. Wchnschr. **24**: 826-827, 1887.
11. Perthes, G.: Schussverletzung der Arteria Pulmonalis und Aorta, Beitr. z. klin. Chir. **19**: 414, 1897.
12. Hankel, Ernst: Stichverletzung der Aorta, traumatisches Aneurysma, Tod 17 Tage nach der Verletzung durch Erstickung, Deutsche Arch. f. klin. Med. **64**: 140-145, 1899.
13. Brentano: Schussverletzung der Aorta, Verhandl. d. deutsch. Gesellsch. f. Chir. **33**: 92-94, 1904.
14. Kratter: Cited by Oberhelman, H. A., and LeCount, E. R.: Peace Time Bullet Wounds of the Abdomen, Arch. Surg. **32**: 373-412, 1936.

15. Berg: Nicht tödliche Schussverletzung der Aorta, Ztschr. f. Med. Beamte **21**: 389-393, 1908.
16. Tegeler: Schussverletzung der Aorta mit eingeheilter Kugel in der Herzklappe, München. med. Wchnschr. **56**: 1740, 1909.
17. Momm: Cited by Oberhelman and LeCount.[14]
18. Minkowski: Schussverletzung der Aorta thoracica, Jahresb. d. schles. Gesellsch. f. vaterl. Kult. **38**: 38-39, 1917.
19. Hulst: Aneurysma spurium aortae abdominalis nach Schussverletzung, Vrtljschr. f. gerichtl. Med. **59**: 108, 1920.
20. Bonnet, Paul: Plaie de l'aorte abdominale pare balle: considérations sur les lésions anatomiques dans leurs rapports possibles avec l'hémostase spontanée, Gaz. d. hôp. **93**: 725-727, 1920.
21. Oesterlein, O.: Traumatic Aneurysm of Abdominal Aorta, Aerztl. Sachverst.-Ztg. **32**: 324-327, 1926.
22. LaRoque, G. Paul: Penetrating Bullet Wound of the Thoracic Aorta Followed by Lodgement of the Bullet in the Femoral Artery, Ann. Surg. **83**: 827-830, 1926.
23. Lubenau: Beitrag zur Ueberlebungsdauer und Handlungsfähigkeit nach tödlicher Verletzung der Aorta ascendens, Ztschr. f. Med.-Beamte **40**: 251-254, 1927.
24. Nissen, R.: Aneurysma des Aortenbogens nach Schussverletzung, Deutsche Ztschr. f. Chir. **211**: 262-265, 1928.
25. Mennyey, G.: Wounds of Aorta, With Varying Periods of Survival of Patient, Arch. di antropol. crim. **52**: 185-202, 1932.
26. Edmundson, K.: Transfixion of Aorta (by Arrow), Brit. J. Surg. **23**: 869-870, 1936.
27. Tesař, J.: Knife Wound of Abdominal Aorta With Fatal Outcome After 11 Days, Časop. lék. česk. **76**: 1495-1497, 1937.
28. Kornblith, B. A.: Gunshot Wound Through the Abdominal Aorta, Ann. Surg. **113**: 637-640, 1941.
29. Pemberton, J., Seefeld, P. H., and Barker, N. W.: Traumatic Arteriovenous Fistula Involving the Abdominal Aorta and the Inferior Vena Cava, Ann. Surg. **123**: 580-589, 1946.
30. Storck, A. H.: Case Report, Ann. Surg. **123**: 607, 1946.

WAR WOUNDS OF THE RECTUM AND ANAL SPHINCTER

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DURING World War II Walter Reed General Hospital was designated as a center for the treatment of wounds involving the rectum and anal sphincter. Harvey B. Stone, civilian consultant in surgery, had direct supervision over the treatment of these patients, made frequent visits to the hospital, examined practically all of the cases, and performed many of the operations personally. The Army is greatly indebted to Stone for thought and energy which he spent to give each man the best possible result in the repair of the injury. Following is an account of the classification, methods of treatment, and results obtained in this group of patients under his direction.

MATERIAL

Forty-one patients with wounds of the rectum and anal sphincter were treated. All except one of the wounds were due to enemy inflicted gunshot wounds, the majority caused by shell fragments or machine gun fire. All patients were between 20 and 36 years of age. In most instances no definitive treatment for sphincter incontinence or external rectal fistula had been given prior to transfer of the patient to this hospital, though in many instances skin grafts, secondary wound closures, and recto-urethral fistula repairs had been performed. One patient had had two previous attempted closures of a large external rectal fistula. The average lapse of time between receiving the wound and the first definitive treatment in this hospital was ten months. This length of time is explained by the fact that most cases were complicated by other injuries which received treatment priority. These included eleven rectovesical or urethral fistulas and numerous instances of sciatic nerve injury, perforations of the colon and small bowel, and compound fractures of pelvic bones. All patients had had débridement of the wounds and most of them a temporary sigmoid colostomy at the time of injury. Most of them had had local application of sulfanilamide crystals and shock treatment in the form of plasma and blood transfusions.

PRELIMINARY TREATMENT AND CLASSIFICATION

On admission each patient was carefully examined, proctoscopy was carried out, the case was discussed, and the injury classified. He was then placed on a regime of sphincter and gluteal muscle exercises and re-examined at weekly intervals for a period of about four weeks before any operative treatment was carried out. This was done because of the striking results which followed these exercises, alone, in many instances. By this routine eleven patients regained adequate sphincter control without operation and the colostomies were closed with satisfactory outcome. The remaining thirty cases fell into five groups: (1) high rectal fistulas not involving the anal sphincter; (2) wounds of the anal sphincter in which part of the muscle was replaced by scar, but the remainder functioned satisfactorily; (3) complete destruction of the sphincter, but

Received for publication, July 14, 1947.

with good perianal tissues and good gluteal muscle function (this group included injuries of the nerve supply of the sphincter, as those which occurred in sacral wounds); (4) complete destruction of the sphincter with additional loss of perianal tissues; (5) complete loss of sphincter, lower rectum, perianal tissues, and gluteal muscles, with extensive scar formation. (By the term "sphincter" is meant the entire muscular mechanism for voluntary control of bowel movements and it includes both the external and internal muscles.)

GENERAL OPERATIVE ROUTINE

All patients were given sulfasuxidine, 5 Gm. every eight hours by mouth and 2 Gm. daily into the lower loop of the colostomy for five days before operation; rectal and colostomy saline enemas were given until clear the night before operation. Except for high rectal fistulas all operations were performed in lithotomy position because that seemed to give better exposure than the prone or jackknife positions. Because of the extensive scarring the difficulty in finding torn ends of sphincter muscle and the danger of breaking into old recto-urethral fistulas, etc., we became thoroughly impressed with the fact that the general surgical principles of good light, adequate exposure, and hemostasis are essential for success in this work.

In determining the end result of treatment several factors were considered. Objectively the result was judged largely by the degree of sphincter function which was detectable on examination and the patient's ability to control liquid and solid bowel movements. Of equal importance, however, was found to be the patient's subjective satisfaction in his result. Many patients who had relatively little sphincter control were able, with the aid of a low residue diet and an occasional low enema, to lead normal economic lives and were well satisfied, while others, with better control, complained bitterly of occasional accidents.

High Rectal Fistulas.—Four patients with external rectal fistulas, above the anal sphincter, were admitted. One extended from the rectum, one inch above the sphincter, backward, around the coccyx to end in a granulating area on the skin. Another (Fig. 1) extended from a wound of entrance just to the right of the sacrum inward to the rectosigmoid junction. These slowly healed completely after thorough curettement of granulation tissue and the rongeuring away of sequestrated bone from the coccyx and sacrum. In the two remaining patients the coccyx and lower sacrum had previously been removed, the fistulas extending straight out from the rectum below the amputated stump of sacrum. These fistulas were closed by a method demonstrated by R. F. Bowers. With the patient in a prone position the external opening of the fistula was excised by a midline elliptical incision. Dense scar tissue was then carefully dissected completely away from the rectal wall for a distance of at least 1½ inches from the fistulous opening on all sides. Bone was rongeured away from the sacral stump until the fistula was quite free. Its edges were then excised and the fistula was closed by a running 00 chromic suture reinforced by interrupted serosal sutures. Large well-vascularized flaps of muscle and subcutaneous tissue were dissected out as far laterally as possible until they could be united in the midline to close

dead space. The skin was closed with silk, leaving a stab wound drain well away from the old fistulous tract. The wounds healed by primary intention in both cases. In one the fistula has now remained closed for six months since closure of the colostomy. In the other the colostomy was closed in August, 1946, but the fistula reopened in October and it was necessary to reopen the colostomy. The fistula has now entirely closed again spontaneously.

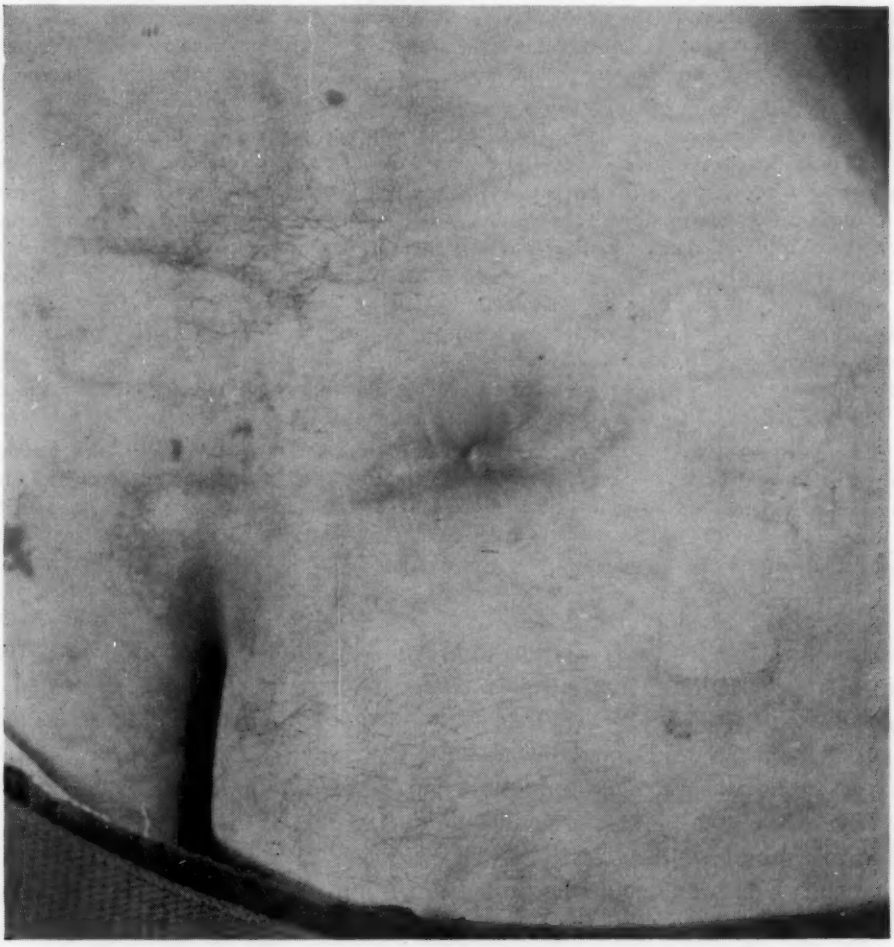

Fig. 1.—High rectal wound resulting in external fecal fistula.

CASE 1.—A 36-year-old private first class of the Infantry was admitted to Walter Reed General Hospital on May 13, 1945. He had been well until Nov. 22, 1944. On that date near Luxemburg he was wounded by enemy machine gun fire which resulted in a wound of the left upper arm with fracture of the left humerus and a gunshot wound in the left hip, the bullet traversing the upper rectum and having its wound of exit through the lower part of the sacrum. He received medical aid six hours after injury and was taken to a battalion aid station, from which he was transferred to the evacuation hospital, arriving on Nov. 22, 1944. There it was found that the sigmoid colon had likewise been perforated. On Nov. 23, 1944, under gas-oxygen anesthesia, closure of the perforation of the rectosigmoid was performed, a Penrose drain placed in the pelvis, and colostomy performed. The wounds gradually healed. He was then sent through air evacuation to the Zone of Interior.

In April, 1945, he began to complain of pain in the left hip and was finally placed in traction with an x-ray diagnosis of osteoarthritis of the left hip. Meanwhile a high rectal fistula had developed in the gunshot wound of exit. An attempt at closure had been made but had not been successful.

Physical examination on admission to Walter Reed General Hospital revealed a markedly emaciated patient lying in bed in a body cast. There was a midline incisional scar and a left-sided double-barreled colostomy functioning well. There was a deep wound over the coccygeal area; it was draining purulent exudate. The anus and rectum appeared normal on inspection. On a digital examination the anal sphincter was normal but there was found to be a direct communication through the coccygeal wound into the rectum. A probe passed through this wound, which was approximately 1 cm. in diameter, could be seen with a proctoscope in the upper rectum.

The rectum was irrigated daily with saline solution and a penicillin pack placed in the external opening of the fistula, but the fistula failed to heal. On Jan. 28, 1946, therefore, under general anesthesia with the patient in a prone position an incision was made excising the fistulous tract, carried down through dense scar tissue to the rectum itself. What appeared to be the third and fourth segments of the sacrum were removed in order to allow better exposure of the fistula. There was dense scar entirely around the opening in the bowel and this was excised. Gluteal muscles and the origins of the sacrospinalis muscles were then carefully dissected backward retaining their blood supply as much as possible until sufficiently large flaps of muscle were formed to cover the defect. The fistula itself was closed by a purse-string suture. With heavy catgut sutures the muscle flaps were imbricated over the defect and the wounds closed tightly except for one cigarette drain.

The postoperative convalescence was uneventful. On Feb. 20, 1946, the wound had apparently completely healed. The patient was walking with the aid of crutches, the left hip being almost entirely ankylosed. In August, 1946, the colostomy was closed by intraperitoneal end-to-end anastomosis. The postoperative course was satisfactory and when last seen the patient was about to be discharged from the Army.

Destruction of Part of Anal Sphincter.—Eleven of the forty-one cases fell into the group with part of the anal sphincter destroyed and were treated surgically. Operative treatment consisted of four steps, all performed as a single procedure (Fig. 2). (1) In lithotomy position an incision was made at or just outside the mucocutaneous border of the anus and usually extended entirely around the anus. Sometimes only one-half of the anal circumference was necessary. The mucous membrane was dissected proximally for 1½ to 2 inches to a point well above the scarred area so that after excision of the scar the mucous membrane could be pulled down and resutured to the skin covering the defect. (2) The scar tissue was excised from the sphincter muscle, skin, and mucous membrane. (3) The ends of the anal sphincter were then carefully dissected out far enough back to allow them to be crossed over, sutured together with several mattress catgut sutures, and anchored to the perianal tissues. (4) The mucous membrane was drawn down and sutured back to the skin with carefully placed interrupted silk sutures. In large defects a small rubber drain was sometimes placed through a stab wound outside the sphincter for a period of forty-eight hours. Postoperatively, hot sitz baths were begun on the fourth or fifth day and the skin sutures removed on the eighth day.

In general, the final results in this group were good. Six of the eleven patients had good sphincter power, could hold liquid or solid bowel movements, and were well satisfied. Three had fairly good sphincter power and could control

water for a short time, solid bowel movements indefinitely. One of these was somewhat dissatisfied with the result. Of the remaining two both had severe injuries. One developed slight sphincter power postoperatively and because of the scarred distortion of the anal canal was able to control solid bowel movements to his own satisfaction. The last of the eleven (Case 3, Fig. 3) entered

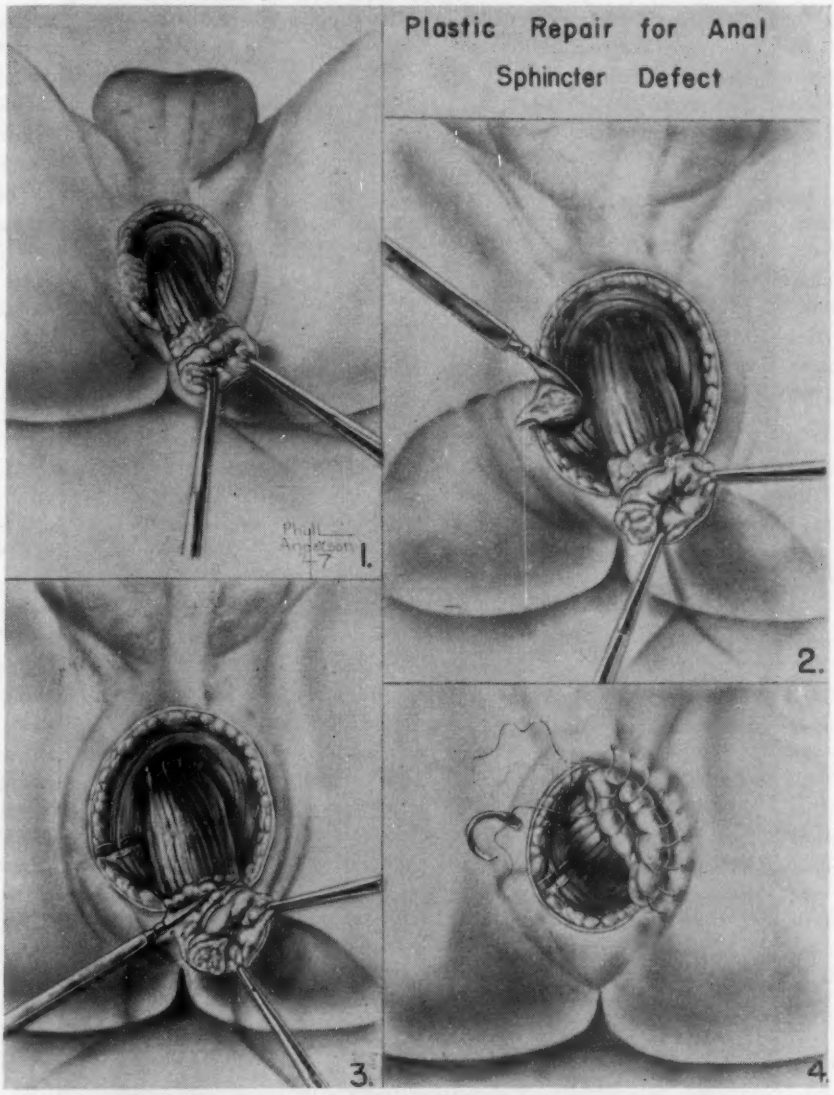

Fig. 2.—*1*, A circular incision has been made around the mucocutaneous border of the anus and the mucous membrane of the rectum dissected upward for a distance of about 1½ inches. Mucous membrane, including scarred area, is drawn downward. *2*, Scar is excised from exposed anal sphincter. *3*, Sphincter muscle has been repaired. Rectal mucous membrane is cut across above scarred area. *4*, Remaining mucous membrane is sutured to skin to cover repaired sphincter.

this hospital with a four square inch defect in the posterior wall of the rectum and an old rectourethral fistula. The rectal defect was closed as a first step. At a later stage an attempt was made to find sufficient muscle to form an adequate sphincter with only partial success. In this procedure the old rectourethral

fistula was inadvertently reopened. At a third stage a Young-Stone plastic repair of the urethral fistula was performed and scar tissue excised. This was successful. He now has slight sphincter control and has a good anus without excessive scarring. The colostomy has not yet been closed.

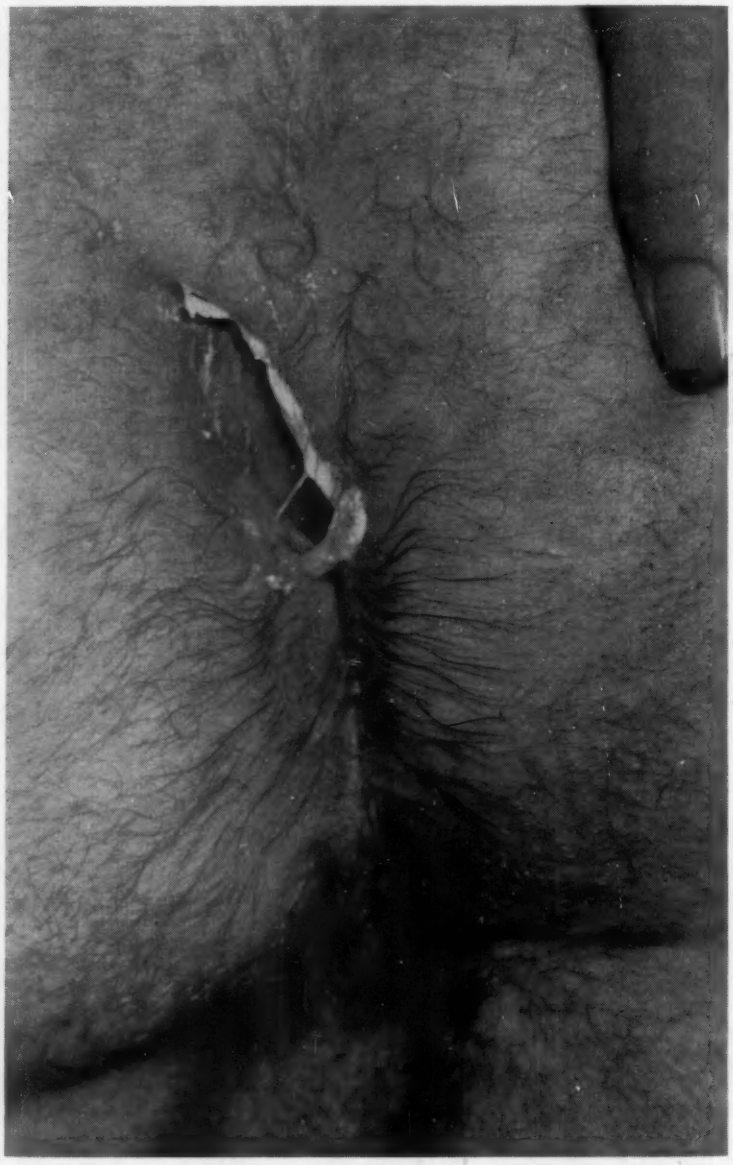

Fig. 3.—Wound causing complete destruction of posterior wall of the rectum and almost the entire anal sphincter.

Case 2.—A 24-year-old corporal of the Engineers, with three years and two months service, was admitted to Walter Reed General Hospital on March 2, 1945. He had been well until Aug. 17, 1944. On that date, while in action against the enemy, near Chartrez, France, he was severely wounded by a shell fragment which produced a penetrating wound of the right buttock on its medial surface, involving the rectum, bladder, terminal ileum, and jejunum.

On the date of injury a laparotomy was performed at an evacuation hospital with resection of twelve inches of mid-ileum and six inches of the lower jejunum with end-to-end anastomosis, repair of the bladder wound, and performance of a lower sigmoid colostomy. Wounds of entrance and exit were débrided. His condition gradually improved and he was transferred through a series of hospitals, arriving at this hospital for definitive care.

Physical examination on admission revealed a left sigmoid colostomy functioning well. There was considerable scarring about the rectum but all wounds were healed. There was a scar on the right side of the rectum which distorted the anal canal. The anal sphincter function was fairly good but was interfered with by this scar. Water injected into the distal loop of the colostomy passed through the rectum and the patient was unable to control it. He was able to partially control barium solution injected into the lower loop of the colostomy. He was given a regime of sphincter muscle strengthening exercises without appreciable improvement in his condition.

On April 7, 1945, under transacral-caudal anesthesia, plication of the rectal sphincter and plastic to the anus were performed. The postoperative course was uneventful and on Aug. 3, 1945, examination showed good sphincter power, no drainage from the rectum, and a well-healed scar. A small amount of scarring was palpable in the upper third of the anus on the right side. Water placed into the lower loop of the colostomy could be held indefinitely. On Aug. 13, 1945, under spinal anesthesia, an intraperitoneal closure of the left sigmoid colostomy was performed. On Aug. 22, 1945, examination showed continued improvement in the function of the sphincter muscle and on Sept. 19, 1945, the patient was discharged from the service.

CASE 3.—On Feb. 23, 1945, on Luzon, Philippine Islands, this Infantry soldier was wounded by machine gun fire sustaining two wounds, one in the right thigh near the groin and the other in the left thigh near the lateral surface. Both of these wounds made their exits through the rectum. He was operated upon that day, a colostomy performed, and the wounds débrided. He was then evacuated through a chain of hospitals, arriving at Walter Reed General Hospital for definitive care.

Physical examination on admission to this hospital was essentially negative with exception of the rectum and perineal area. There was a large open defect lying between the tip of the coccyx and the anterior border of the anal sphincter through which the anterior wall of the rectum was exposed over an area of about two inches in diameter (Fig. 3). The posterior wall of the rectum was entirely absent to that extent. No sphincter action whatever was demonstrable. A urethral fistula which had been present previously was healed. The colostomy was functioning well.

The wound was treated by daily wet dressings. Examination on Oct. 20, 1945, showed a clean wound with no sinus or fistula and it was felt that some degree of movement of the sphincter could be detected. The large defect in the posterior rectal ampulla appeared to be unchanged. In November, 1945, under satisfactory spinal anesthesia, the edges of the large defect were excised with the removal of a large amount of scar tissue. The rectum was then carefully freed from the overlying tissues entirely around the defect to a sufficient degree so that the rectum could be closed and the skin closed over the defect leaving only a small opening for the anus. This wound healed well.

In February, 1946, an attempt was made to restore anal sphincter function. Scarring was so dense, however, that although the sphincter muscle was found and could be brought around the anus, it was impossible to free the mucous membrane sufficiently to bring it outside the newly formed anus to prevent further scar formation. In dissecting free the scar tissue anteriorly the old urethral fistula was inadvertently broken into. A urethral catheter was placed in the urethra and the patient returned to the ward. Postoperative convalescence was somewhat stormy because of the development of cystitis. However, the anal sphincter thus formed functioned satisfactorily and a definite degree of contraction was discernible. Water placed in the lower loop of the colostomy could only be slowed and could not be definitely stopped by the new sphincter. The posterior drainage on removal of the catheter decreased to only a few cubic centimeters a day and the wound slowly healed.

In November, 1946, another attempt at dissection of mucous membrane of the rectum upward was made successfully, the urethral fistula was closed, and a satisfactory anus resulted. There is now some detectable sphincter function. The colostomy has not yet been closed. A fascial sling plastic procedure is being considered to provide more effective sphincter function.

Complete Sphincter Loss With Good Perianal Tissues.—Patients with no sphincter action but good gluteal muscle action if not complicated by excessive scar or stricture formation were found to be suitable candidates for the Stone

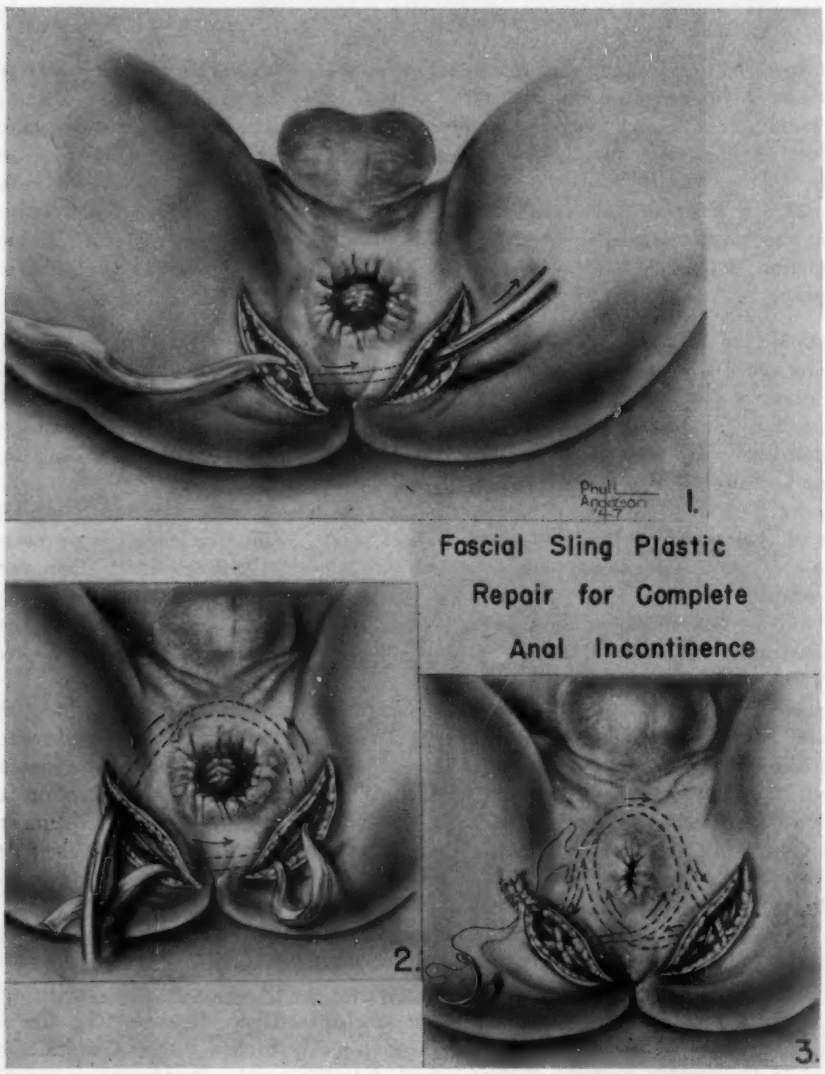

Fig. 4.—*1*, Short incisions have been made on each side of anus posteriorly, exposing lower edge of gluteus maximus muscle. A strip of ox fascia is pulled through posterior subcutaneous tunnel from one incision to the other. *2*, End of the strip is drawn back through anterior subcutaneous tunnel, passed through a portion of gluteus muscle, and tied to the distal end of the same strip, forming a sling around one side of the anus. *3*, Beginning at the opposite incision a second strip of fascia is passed in the opposite direction and tied in a similar way completing the circle. The skin is closed with silk.

type of fascial plastic operation.* These cases were difficult problems at best. Although the operation did not insure good sphincter function in all instances it often made the difference between total incontinence and sufficient control for a reasonably normal life. The Stone fascial repair was performed nine times in eight patients, one repeat operation being necessitated by sloughing out of the first strip of fascia. With the patient in lithotomy position (Fig. 4) 3 cm. incisions were made posterolateral to the anus on each side. These were carried down to the medial border of the gluteus maximus muscle. By blunt dissection with a curved Kelly clamp a tunnel was made in the subcutaneous tissues around the anus anteriorly connecting the two lateral incisions. A similar tunnel was made posteriorly. Care had to be exercised not to make these tunnels too close to the mucous membrane of the rectum or to the skin for fear of the fascial strips sloughing through. Anteriorly there was danger of breaking into old recto-urethral fistulas. When the tunnels had been completed a strip of ox fascia was slipped through the anterior tunnel from left to right, then the end returned through the posterior tunnel from right to left. A similar strip was placed beginning from the right side. Thus a double noose purse string was formed. Each loop was passed through a large bite of gluteus maximus muscle and tied tightly enough to produce a definite sphincter effect but not tightly enough to slough through the mucous membrane of the rectum. Careful aseptic technique was essential. Penicillin in oil, 300,000 units daily, was given for seven days postoperatively. Fascia lata has been used in some cases by Stone, but he has reported ox fascia to be equally effective.

CASE 4.—A 23-year-old private of the Armored Force had been well until Aug. 31, 1944. On that date, while on reconnaissance duty, he was captured by the enemy in France. Some time later Americans appeared and this soldier and the men with whom he had been captured were shot in the back by pistol fire by the Germans. He was hit by two bullets. One penetrating the right buttock posteriorly made its exit anterior to the tuberosity of the ischium. The other struck him in the perineum, anus, scrotum, and rectum, resulting in avulsion of the left testis and severe injury to the perineum, anus, and rectum with perforation of the posterior urethra and rectum. He was taken to a field hospital and on Sept. 1, 1944, a colostomy, suprapubic cystotomy, laparotomy, left orchidectomy, and débridement of the perineum were performed. He was transferred to a general hospital in England where it became evident that there was a recto-urethral and rectoperineal fistula. He arrived by transfer at the Walter Reed General Hospital April 24, 1945.

Examination on admission revealed a functioning double loop colostomy, suprapubic cystotomy, and a perineal scar with a 1 cm. fistulous tract opening from which purulent fluid could be expressed. There was some anal sphincter tone posteriorly and considerable stenosis of the anal orifice. He developed nephrolithiasis which was treated conservatively until August 21, when a left pyelotomy and nephrolithotomy were performed. On Jan. 29, 1946, a Young-Stone repair of the recto-urethral fistula was performed. The patient was transferred to the General Surgical Service.

Examination on transfer revealed a tight fibrous band at the mucocutaneous border of the rectum, considerable fibrotic scarring of the anal canal, and slight weak anterior sphincter action. Because of the fact that this sphincter action was nearly absent it seemed improbable that any sphincter could be successfully brought around the anal canal to function satisfactorily. Therefore, since the gluteal function was good, it was felt that a fascial strip plastic

*Stone, H. B., and McLanahan, S.: Results With Fascia Plastic Operation for Anal Incontinence, Ann. Surg. **114**: 73-77, 1941.

operation would be feasible. On Feb. 21, 1946, this was done under sacral anesthesia. The postoperative course was satisfactory and on the seventh postoperative day there was some definite sphincter action on contraction of the gluteus maximus muscles. The sigmoid colostomy was closed. Sufficient sphincter action was present for control of liquid and solid bowel movements.

CASE 5.—A corporal of the Infantry was admitted to the Walter Reed Hospital on March 10, 1945, because of a lacerated wound of the anus and rectum. He had been well until June 16, 1944. On that day near St. Lo, France, he was wounded by enemy machine gun fire sustaining a severe lacerated injury of the right and left buttocks and perineum with penetration of the anus, rectum, and membranous urethra and a fracture of the left ischial tuberosity. These injuries were followed by a chronic perineal-urethral fistula. He received emergency treatment in the form of débridement of wounds, suprapubic cystotomy, and later a sigmoid colostomy on June 17, 1944, at an evacuation hospital. He was evacuated to the United States on Nov. 2, 1944, and transferred to Walter Reed General Hospital.

On admission examination revealed considerable scarring of the anal canal with a very hard ridge of scar tissue posteriorly and a softer, thinner narrow ridge of scar tissue anteriorly. The examining finger could be inserted only about 1½ to 2 cm. into the anus because of the dense scarring. The urinary fistula had closed. On April 1, 1945, examination revealed very little sphincter control and since no sphincter muscle could be felt it was decided that a fascial sling operation should be performed. On July 7, 1945, this was done. Examination on Aug. 2, 1945, still showed considerable scarring but a very slight constriction of the canal was produced when the patient tightened the gluteus maximus muscles. On Sept. 2, 1945, examination showed fair anal constricting power and it was decided that the colostomy should be closed and at the same time the rectum dilated to two fingers at operation. The colostomy was closed under spinal anesthesia as an end-to-end intraperitoneal anastomosis and the rectum dilated. Postoperatively he was able to control solid bowel movements fairly satisfactorily, liquid movements only partially. He was discharged from the service on a certificate of disability.

Complete Sphincter Loss With Damage to Perirectal Tissues.—The group with complete sphincter loss with daamge to perirectal tissues was similar to the preceding one except for the fact that damage to perianal tissues made a preliminary plastic operation necessary before fascial strips could be introduced with safety. There was only one patient of this type in whom the coccyx had been removed and nothing remained over the posterior aspect of the rectum except skin. Through a midline posterior incision flaps of subcutaneous tissue were mobilized laterally and brought together in the midline between rectum and skin. At a later operation fascial strips were successfully placed around the anus.

CASE 6.—A 26-year-old Infantry soldier had been well until June 1, 1944. On that date while in action in Italy he was wounded by shell fragments in the area posterior to the rectum. A left sigmoid colostomy was performed. A urinary fistula later developed from the urethra into the rectum. On admission to the Walter Reed General Hospital the wound had healed entirely. He had good gluteal muscle function but no function of the anal sphincter whatsoever. After admission to Walter Reed Hospital a Davis-Stone repair of the urethral fistula was performed. When the patient was transferred from the urologic to the general surgical section his only complaint was complete paralysis of the anal sphincter due apparently to interference of the nerve supply of the sphincter because of the shell fragment wound. As a result of this wound examination on May 15, 1945, revealed only a thin scar posteriorly between the rectal mucosa and the skin. No sphincter action was discernible and it was felt that this patient would require a fascial strip operation to produce sphincter action. It was believed,

however, that first excision of the scar posterior to the anus should be performed with the bringing of a fat and fascia layer between the skin and the rectal mucosa. On July 28, 1945, under satisfactory inhalation anesthesia, the old scar was excised, and subcutaneous tissue and fascia were interposed between skin and rectum. The skin was closed with interrupted silk sutures. This procedure healed well but because there was no return in sphincter function, on March 12, 1946, under satisfactory spinal anesthesia, a Stone type of ox fascia sling plastic sphincter was performed. The wound healed satisfactorily and on April 1, 1946, the patient was able to hold water for about two minutes when the latter was placed in the lower loop of the colostomy. When last seen the colostomy had not yet been closed.

Two of the eight patients in whom fascial plastic operations were performed had good or fairly good postoperative sphincter power, were able to control liquid as well as solid bowel movements, and were classified as having good results. Five had some contractile power and of these one could hold water for a short time and two were unable to hold water but could control solid bowel movements. The other two had not been tested in the ability to control water but could control solid bowel movements. The one remaining patient had no contractile power at all and could not control water or liquid bowel movements. This patient had only slight gluteal function on one side and none on the other. Due to scarring and obliquity of the anal canal, however, he rarely soiled himself and having been very much depressed when he entered this hospital was truly happy over the final result. All but two of the eight patients in this group were satisfied with their repairs.

TABLE I. RESULTS OF TREATMENT IN SPHINCTER INJURIES

TYPE OF TREATMENT	NUMBER OF CASES	SPHINCTER ACTION			HOLD WATER	HOLD FECES	PATIENT SATISFIED
		GOOD	FAIR	POOR			
Sphincter exercise only	11	10	1	0	11	11	10
Sphincter repair	10	6	2	2	7	9	9
Fascial sling plastic	8	2	5	1	3	8	6
Excision of scar and pull-through	1	0	0	1	0	1	Fairly

Complete Sphincter Loss With Extensive Scarring and Loss of Gluteal Function.—The patients with complete sphincter loss with extensive scarring and loss of gluteal function, the most severely wounded of all, comprised the group for which no satisfactory sphincter repair could be devised. Repairs of the preceding types were attempted but without success. The question then arose as to the type of treatment which would best enable these patients to lead relatively normal lives. This varied somewhat with the opinions of the surgeons and the wishes of the patients. Of the seven who fell within this category the first four were treated by converting their loop colostomies into end abdominal colostomies and resecting the remainder of the sigmoid and the scarred rectum by a Miles abdominoperineal resection. This rid the patients of a mucous seeping uncontrollable perineal colostomy. Because of the slight possibility that in the future some method might be devised of giving such patients a satisfactory perineal anus, three were treated conservatively. In one a pull-through perineal operation was performed with excision of the scarred area of the rectum and production of a perineal colostomy. In the remaining two no perineal surgery was performed. One of these was discharged with the

loop sigmoid colostomy untouched. The other had the abdominal colostomy closed producing a perineal colostomy. In all such patients regular bowel habits, a low residue diet, and occasional low saline enemas were found to contribute materially to the management of the colostomies, whether perineal or abdominal.

The four patients with abdominoperineal resections and one with an open loop colostomy accepted the abdominal colostomies well. The two patients discharged with perineal colostomies were, on the whole, disappointed and may require abdominoperineal resections at a later date.

CASE 7.—This private in the Infantry was wounded in action by shell fragments in Italy during the fall of 1944, sustaining a severe lacerated wound of the perineum and anal region with loss of muscle from both buttocks, exposing the sacrum and fracturing the tip of the sacrum. The lower rectum and anus were traversed by the fragments and the patient was admitted to an evacuation hospital in shock. The wound was débrided, he was given large amounts of blood and plasma intravenously, and a left sigmoid colostomy was performed. After a long period of convalescence he was transferred through several general hospitals, finally arriving at Walter Reed General Hospital in July, 1945.

Examination on admission revealed extensive scarring over the dorsum of the sacrum, in both buttocks and in the anal region. The sacrum had been covered by a skin graft which was very thin. No function of either gluteus maximus muscle was discernible and there was so much scarring of the anal region that not even a probe could be admitted into the rectum. He was seen in consultation and it was felt because of the absence of any contractile power either of the gluteus maximus muscle on either side or of the sphincter and the loss of the lower part of the rectum that an abdominoperineal resection of the lower sigmoid and rectum should be performed. Consequently, after preparing the patient with sulfasuxidine an abdominoperineal resection of the rectosigmoid was performed in August, 1945. The entire lower rectum was found to be replaced by scar tissue and the rectum was removed with considerable difficulty without injury to the urethra. An end colostomy in the left lower quadrant was performed. The wound healed satisfactorily and quite quickly and the left sigmoid colostomy functioned well. The only complaint of the patient was thinned-out tissue over the sacrum. He preferred, however, to have no further surgical operations at the time and was discharged from the Army.

CONCLUSION

The classification and treatment of these forty-one rectal war wounds and the evaluation of the results of the various operative procedures employed has convinced us of several facts: (1) sphincter muscle exercises are of great value in improving anal sphincter power; (2) the best operative results are usually obtained in those cases in which torn muscle ends can be approximated, even though not perfectly; (3) the Stone fascial plastic operation has a definite place in the treatment of such patients if the sphincter ends cannot be found. This operation has given enough control to restore many men to fairly normal lives; (4) when no repair of sphincter power can be devised an abdominoperineal resection is probably the procedure of choice. It must be remembered, however, that this precludes any later repair based upon future developments in rectal surgery.

A CANNULA FOR PANCREATIC FISTULA

A Device for Permitting Complete Periodic Experimental Collection of Pancreatic Juice

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THE study of pancreatic function in disease of the upper gastrointestinal tract has led to various experimental approaches to complete pancreatic fistulas in the surgical laboratory. It is evident from reviewing the literature that the preparation of permanent pancreatic fistula in a dog is a procedure that requires great patience on the part of the surgeon and diligent postoperative care. Those of us willing to undertake the care of such a preparation must remember Elman and McCaughan's classical observation that total drainage of pancreatic juice to the exterior resulted in the death of dogs in seven or eight days. This was true only if the entire output of the external secretion was excluded from the intestine.

In our laboratory, during the course of various studies on the etiology and treatment of peptic ulcer, it became necessary to prepare total pancreatic fistulas. It is the purpose of this paper to present a method by which such a preparation may be attempted and which lends itself to more prolonged experiments with a minimum of care and expense.

TYPES OF PANCREATIC FISTULAS THAT HAVE BEEN PROPOSED

Pavlov[2] described a fistula similar to Heidenhain,[3] in which an oval piece of duodenal wall bearing the orifice of the main duct is dissected out and transplanted into a slit on the abdominal wall. The opening of the bowel is then closed and the duodenum maintained against the anterior abdominal wall by temporary suspension sutures. In his classical description, Pavlov told of the use of rooms in which the floors are covered with sawdust and sand on which the animals may lie, allowing the pancreatic juice to be absorbed and thus preventing digestion of the skin by this juice. These fistulas are not complete, for in the dog the smaller pancreatic duct is important functionally, and in fact empties in association with the common bile duct.

Methods which make use of cannulas leading from the pancreatic duct to the anterior abdominal wall have been proposed by Bernard,[4] Ludwig,[5] and Fodera.[6] These preparations, however, allow for the escape of only part of the juice; moreover, the cannulas fall out.

Lattes,[7] in 1912, proposed a technique similar to Pavlov's. The ducts are brought out through the muscular walls. When the muscles contract, the secretions can thus be held back when not in use. In order to use this type of fistula,

The researches upon which this presentation is based were supported by the Robert A. Cooper Fund for Surgical Research, the Dr. and Mrs. Harry B. Zimmerman Fund for Experimental Surgical Research, and the Dr. Berenice Moriarity Fund.

Received for publication, June 10, 1947.

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a cannula is inserted periodically. However, it is to be noted that the ampulla behind the external opening soon becomes dilated, as are the other ducts.

Frouin[8] attempted to bring the duodenum into the anterior abdominal wall. When sufficient fixation occurs, the duct is transplanted to the skin. Intestinal obstruction results, in addition to intestinal fistulas.

In 1922, Inlow[9] presented a method in which the duodenum is brought subcutaneously; the ducts are finally severed at a subsequent operation and brought externally. An attempt is made to sever all other small vessels and ducts immediately around the main duct. He employed an incision which is curved away from the duct; it was Inlow's contention that this maneuver will prevent obstruction and cicatrization as occurred in Frouin's experiments.

Elman and McCaughan[10] used the method of major pancreatic duct intubation, very much after the method of Rous and McMaster.[11] In their method, the minor pancreatic duct is cut and avulsed. The major duct is then cannulated, and the end attached to a long catheter. This tube is brought out through the flank and connected to a glass T tube, at one end of which a sterile rubber balloon is attached. The other end of the glass tube is used for emptying the balloon of its contents daily. Stringent aseptic precautions are necessary and therefore all joints are covered with gauze soaked in 5 per cent phenol. Again the problem of the cannula slipping out is presented.

More recently, Dragstedt, Montgomery, and Ellis[12] described a method which lends itself to more prolonged experiments. This method consists of transforming that portion of the duodenum with the pancreatic ducts emptying into it, into a closed loop. This duodenal sac is then cannulated by means of a gold-plated cannula which is led to the outside and carefully wrapped in omentum. The common duct is transplanted and the stomach is joined to the lower duodenum by means of a gastroduodenostomy. The total pancreatic juice is then collected in sterile rubber bags. The entire pancreatic secretion is thus lost to the outside at all times. These animals must be cared for rather intensively. Intravenous feeding or return of the pancreatic juice orally must be accomplished, otherwise the dogs will succumb.

In 1940, Bolydreff and Thompson[13] described a method of preparing a pancreatic fistula in which a glass cannula is placed directly into the major pancreatic duct transduodenally. A rubber catheter, which is attached to the glass cannula on the one end and a string on the other, can be brought in and out of the duodenum via a duodenal fistula which is prepared simultaneously. Thus, when the dog is not in use the pancreatic juice is within the intestine. The glass cannulas generally slip out and this may terminate an experiment.

A PERMANENT CANNULA METHOD FOR PANCREATIC FISTULA

In trying to evaluate the various types of pancreatic fistulas, it was decided that the type of fistula proposed by Dragstedt, Montgomery, and Ellis, in which the duodenum containing all the pancreatic ducts was used as a conduit, was the best in principle. However, since this type of procedure allowed for a continuous external loss of secretions to meet this objection, a new type of cannula

was devised, which would allow for external collection of pancreatic juice when necessary, and at other times would allow for drainage into the distal intestine, thus preventing the fatal effect of total loss of pancreatic juice. The cannula, itself, as used in our laboratory, was constructed of stainless steel.* (Fig. 1.)

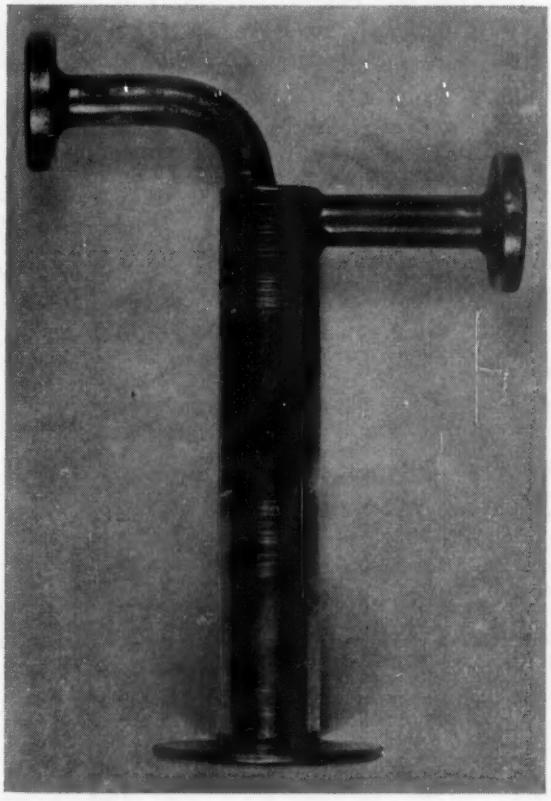

Fig. 1.—Permanent pancreatic cannula, constructed of stainless steel (full size).

Its use is best described by a diagrammatic sketch (Figs. 2 and 3). The common duct is carefully isolated as it enters the duodenum and is ligated and cut. The proximal end is then either transplanted to the stomach or intestine or ligated permanently, and an external biliary fistula is created by inserting a mushroom catheter into the gall bladder and bringing it out through a separate stab wound. The duodenum is then cut across about 2 cm. distal to the pylorus, and again just below the entrance to the lower pancreatic duct. The proximal end of the duodenal sac is then inverted and closed, while one flange of the cannula is placed in the other end. A purse-string type of inversion is then made to secure this in place. This latter procedure is then repeated, with the distal flange being placed and secured into the distal segment of duodenum, which is continuous with the intestinal tract. The continuity of the gastrointestinal tract is then re-established by an aseptic end-to-side anastomosis of stomach to duodenum distal to this flange. Omentum is carefully wrapped

*By Mr. John Phelan of the Scientific Apparatus Division of the University of Minnesota.

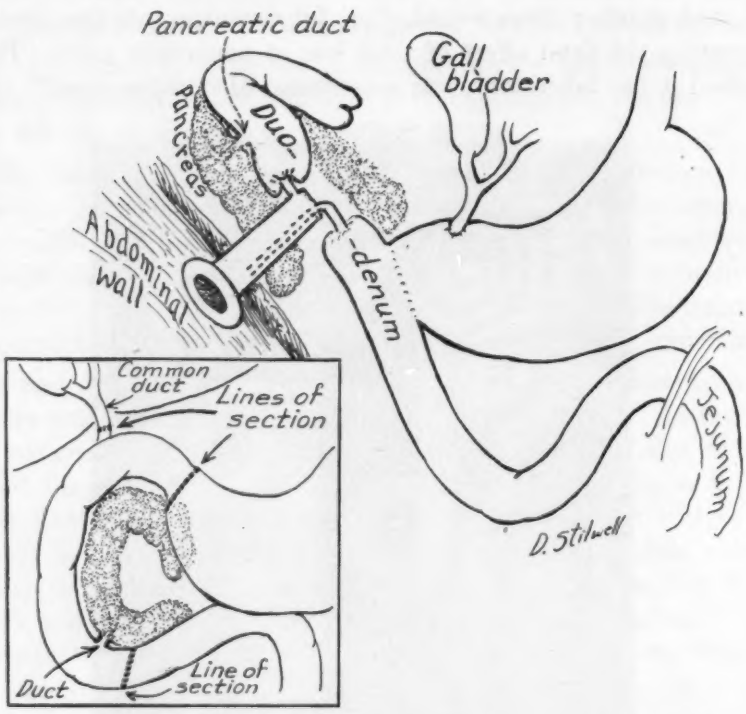

Fig. 2.—Small inset shows the lines of section of the duodenum and commonn bile duct. The common duct is carefully isolated as it enters the duodenum and is ligated and cut. The proximal end is transplanted to the stomach or duodenum. The duodenum is then cut across about 2 cm. distal to the pylorus, and again just below the entrance of the lower pancreatic duct.

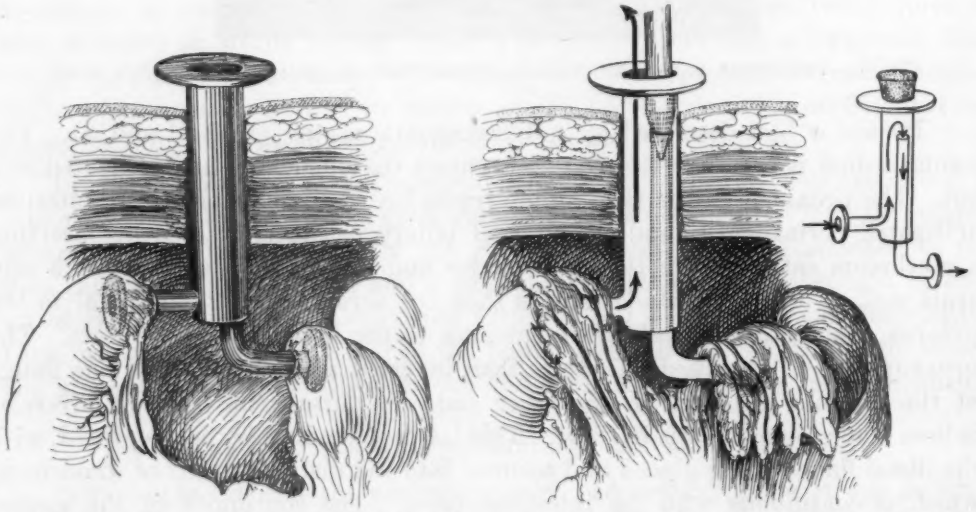

Fig. 3.—The method of placement of the pancreatic cannula. Left, placement of flanges into both proximal and distal portions of the duodenum. Purse-string types of inversions are used to secure this in place. Omentum is carefully wrapped around the metal cannula and this is then led to the outside through a stab wound. Right, direction of flow of pancreatic juice when preparation is being used. Small inset shows direction of flow of pancreatic juice when the animal is not actively employed in an experiment.

around the metal cannula and this is then led to the outside through a stab wound. The duodenal sac is fixed to the parietal peritoneum around the stab wound with a few sutures.

When in use, a small wooden plug is inserted into the inner opening within the cannula. This will prevent any reflux of juice from the intestinal tract proper. When not in use, a rubber stopper is inserted into the main cannula opening. This stopper is about 2 mm. thick and is flush with the external opening. This will prevent the animal from pulling it out and will allow for flow of pancreatic juice into the intestinal tract.

This preparation has been used in four animals with good results. Two of the animals were sacrificed after four months. Post-mortem examination showed the omentum had securely fixed the entire apparatus to the anterior abdominal wall with no leakage around it. One animal died of peritonitis due to leakage at the duodenal entrance of the cannula. The last animal had had an extensive gastric resection (95 per cent), a total biliary fistula, and a complete pancreatic fistula. This animal died after four months because of an accidental introduction into the intestinal tract of concentrated hydrochloric acid. All of the animals were fed normally with kennel ration and table scraps without the use of intravenous or subcutaneous feeding. Supplementary vitamins or bile salts were added to the diet as was deemed necessary.

SUMMARY

A method of total pancreatic fistula preparation is presented. This procedure offers the use of a metal T-shaped cannula which will allow for the selective removal of pancreatic juice, and the automatic return to the intestinal tract of this fluid when the animal is not actively employed in an experiment. The care of animals with pancreatic fistulas is much simplified by this procedure.

REFERENCES

1. Elman, R., and McCaughan, J. M.: Fatal Effect of Complete Loss of Pancreatic Juice, Proc. Soc. Exper. Biol. & Med. **24**: 99, 1926.
2. Pavlov, I. P.: The Work of the Digestive Glands, second English edition, Philadelphia, 1910, J. B. Lippincott Company, pp. 4-10.
3. Heidenhain Quoted in Pavlov.[2]
4. Bernard Quoted in Pavlov.[2]
5. Ludwig Quoted in Pavlov.[2]
6. Fodera, Ph.: Permanente Pankreasfistel. Untersuchungun zur Naturlehre der Menschen und der Tiere, 1896, p. 16, 79.
7. Lattes, L.: Eines Methode Zur Herstellung Kontinenter Pankreasdauerfisteln, Ztschr. f. Biol. Techn. W. Method. **2**: 366, 1912.
8. Frouin, A.: Nouvelle technique de la fistule pancreatique permanente. Presentation d'animaux et de pieces, Compt. rend. Soc. de biol. **74**: 1283, 1913.
9. Inlow, Wm. DeP.: A Technique for the Establishment of a Permanent Pancreatic Fistula With the Secretion of Inactive Proteolytic Ferment, J. Lab. & Clin. Med. **7**: 86, 1922.
10. Elman, R., and McCaughan, J. M.: Collection of Entire External Secretion of Pancreas Under Sterile Conditions and Fatal Effect of Total Loss of Pancreatic Juice, J. Exper. Med. **45**: 561-570, 1927.
11. Rous, P., and McMaster, P. D.: Method for Permanent Sterile Drainage of Intra-abdominal Ducts as Applied to Common Duct, J. Exper. Med. **37**: 11, 1923.
12. Dragstedt, L. R., Montgomery, M. L., and Ellis, J. C.: New Type of Pancreatic Fistula, Proc. Soc. Exper. Biol. & Med. **28**: 109, 1930.
13. Boldyreff, W. N., and Thompson, O. E.: A New Type of Permanent Pancreatic Fistula, Permitting the Regulation of the Outflow of the Secretion, Tohoku J. Exper. Med. **38**: 581, 1940.

VERRUCOUS CARCINOMA OF THE ORAL CAVITY

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DURING the past seven years, we have noted a variety of squamous carcinoma whose behavior is unique and which has a typical clinical course with characteristic gross and microscopic findings. We have designated this type of squamous carcinoma as verrucous carcinoma and feel it should be separated from other epidermoid carcinomas for, even when extensive, with proper treatment the prognosis is excellent.

We have seen 31 patients; 26 were men and 5 were women. The majority of these patients were rather aged, the average age being 67 years (25 were over 60 years of age, and 13 of these were over 70). There was only one patient under 57 years. This patient was a woman of 41 years, with a lesion of the buccal mucosa; case history revealed that she was a tobacco chewer.

Tobacco chewing was probably a most important factor in the etiology of these lesions. Eleven of the 18 patients with lesions of the buccal mucosa were inveterate tobacco chewers. Seven of these patients also had lesions associated with leucoplakia. Friedell and Rosenthal* reported 8 patients with buccal mucosal and lower gingival lesions of verrucoid character in which tobacco chewing was thought to be an important etiologic factor. Over one-half of the patients reported here had poorly fitting dentures, poor oral hygiene, and carious and jagged teeth.

The lesions were distributed as follows: 18 were of the buccal mucosa; 8 of the lower gingiva; 1 of the upper gingiva; 2 of the hard palate; 1 of the tongue, and 1 of the tonsil. It was difficult to estimate clinically the duration of these lesions, but often they had been present for considerably over one year, and growth was relatively indolent.

As the lesions gradually increased in size to extend over a fairly large area, the patients not too infrequently complained of pain and difficulty in mastication, but there was seldom any bleeding. When the tumor arose in the region of the buccal mucosa, it tended to extend into the buccal gingival gutter. As it extended in surface area, it also locally invaded contiguous structures. It may grow into the cheek, even ulcerate on its surface (Fig. 1), may grow out to form a mass beneath the mandible (Fig. 2), and even grow from within the oral cavity to implicate the buccal commissure (Fig. 3). As the verrucous carcinoma frequently arises on the lower alveolus or extends into the buccal gingival gutter, it grows into the soft tissues overlying the mandible and quickly becomes fixed to the periosteum. With increased growth plus infection, it gradually destroys periosteum and directly invades and even destroys a considerable portion of the mandible (Figs. 4 and 5). Because of concomitant

Received for publication, June 21, 1947.

*Friedell, H. L., and Rosenthal, L. M.: The Etiologic Role of Chewing Tobacco in Cancer of the Mouth, J. A. M. A. 116: 2130-2135, 1941.

infection, the draining lymph nodes (particularly submental and submaxillary) frequently become enlarged and are invariably tender. This enlargement often leads to an erroneous diagnosis of metastatic carcinoma. The papillary lesions present a characteristic, somewhat pebbly, mammillated surface. The tumor may be relatviely soft, but with coexisting infection induration becomes prominent.

When these lesions are surgically resected, filmy leucoplakia may be found associated with them and invariably the often extensive lesion is piled up in rugal folds with deep cleftlike spaces between them (Figs. 6, 7, 8, and 9). If the tumor is cut into, it is often seen extending in the deeper tissues, and when deeply invasive it is associated with considerable infection.

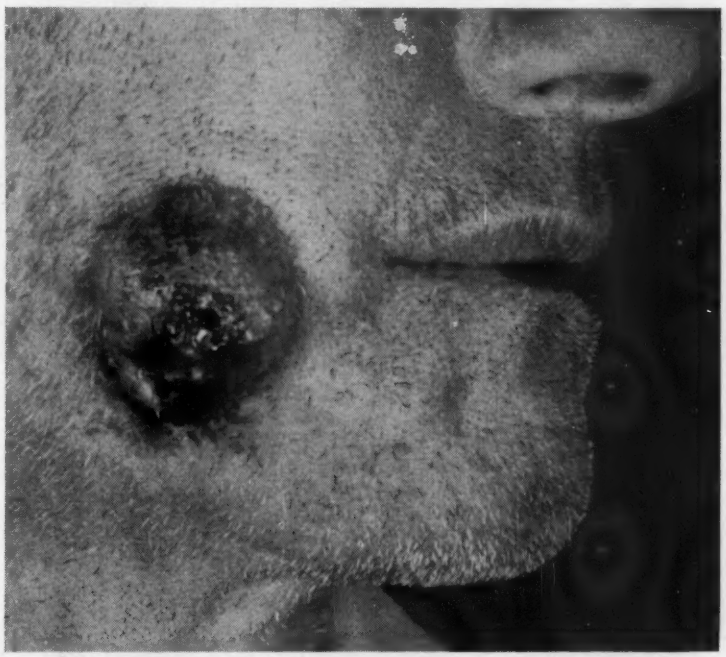


Fig. 1.—Verrucous carcinoma of buccal mucosa invading skin of cheek.

Microscopically there is often a rather rough transition between somewhat atrophic epithelium and the process. The first change noted is a piling up of keratin on the surface, with beginning downgrowth of fingers of epithelium (Fig. 10). As the process continues, club-shaped fingers of hyperplastic epithelium gradually push rather than infiltrate their way into the deeper tissues (Fig. 11). It should be emphasized that this epithelium is well differentiated and that the basement membrane remains intact. With further growth, the pattern becomes somewhat more complicated as more of the surface becomes involved. Cleftlike spaces with degenerating keratin project rather deeply. As the epithelium grows, the central portion of the fingers becomes well differentiated and finally undergoes cystic degeneration (Fig. 12). There is a

wall of inflammatory tissue which is coexistent with the lesion and is present beyond it. This inflammation is made up of connective tissue, plasma cells, mononuclears, and, rarely, focal abscesses. The tumor gradually extends, but its invasion of other structures is probably considerably influenced by the presence of the accompanying inflammatory process. The local invasive qualities are prominent and any contiguous structure such as cheek, soft tissues in the submaxillary area, mandible, or antrum can be invaded. However, it is unique that

Fig. 2.—Local recurrence following partial mandibular resection. (The only case of such recurrence. This patient had been treated previously by irradiation.)

Fig. 3.—Verrucous carcinoma extending from within the oral cavity to implicate the buccal commissure.

although the tumor may grow in the immediate proximity of lymph nodes, it invariably grows around them rather than metastasizing to them. Although in 10 instances the extensiveness of the tumor necessitated partial or complete mandibular resection with upper neck node dissection, in only one patient was a regional node involved by direct extension and in only one other patient recently seen was a single high metastatic node implicated. In no instance have distant metastases appeared.

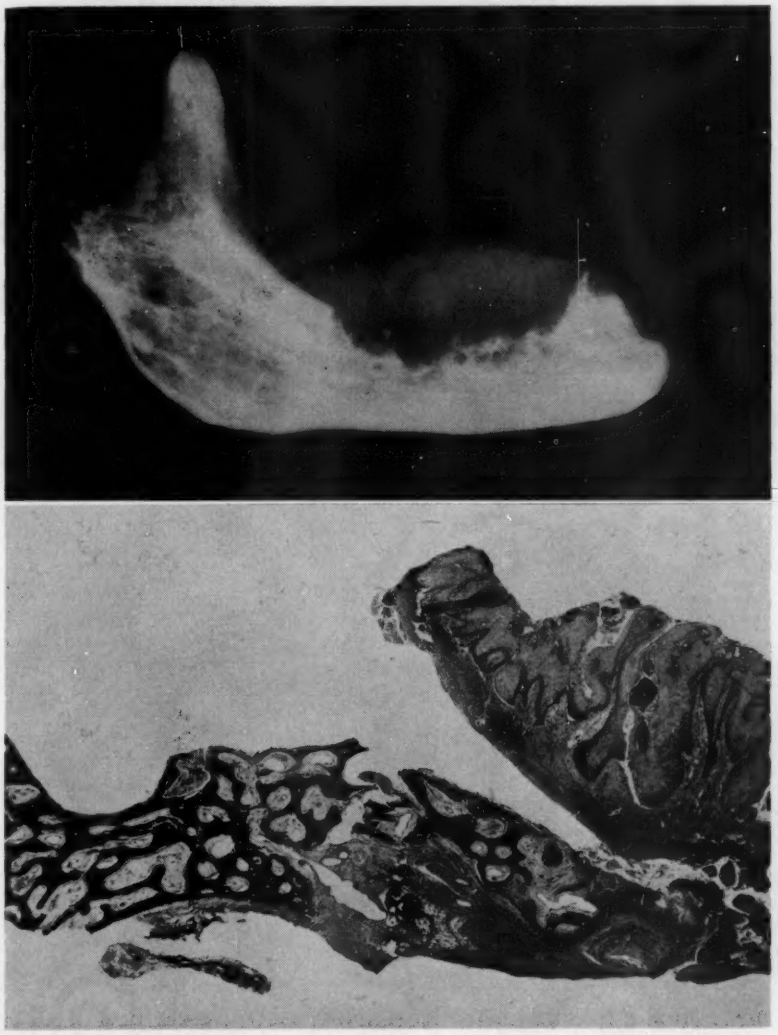
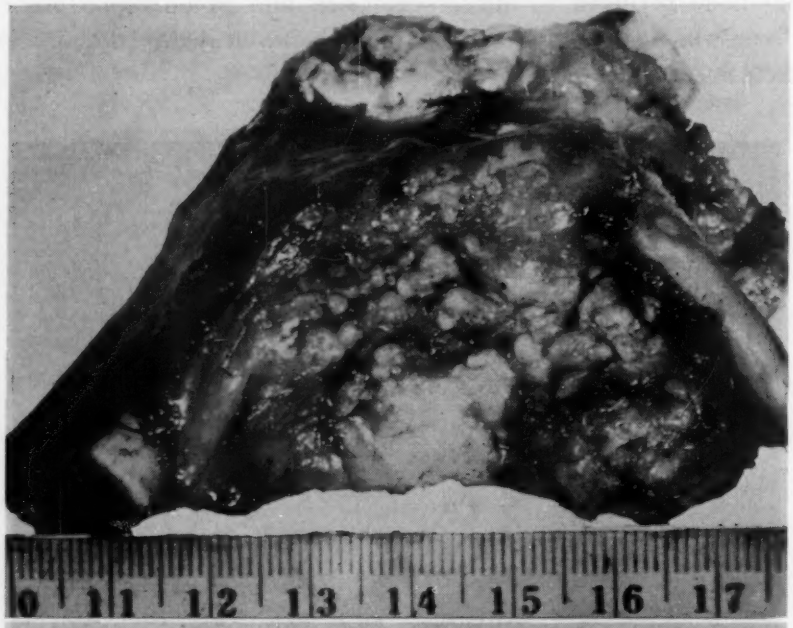


Fig. 4.—Extensive secondary destruction of the mandible.
Fig. 5.—Replacement of the mandible by verrucous carcinoma (very low power).

Friedell and Rosenthal reported 8 cases which apparently fall into this group, for the lesions described by them occurred in aged men on the buccal mucosa and lower gingiva. The lesions were described as papillary verrucoid in character and, although often extensive, only one out of 8 metastasized. They

were treated by irradiation and this was immediately successful in controlling the disease. However, the longest follow-up was two years, and most of the other surviving patients had been followed six months or less.



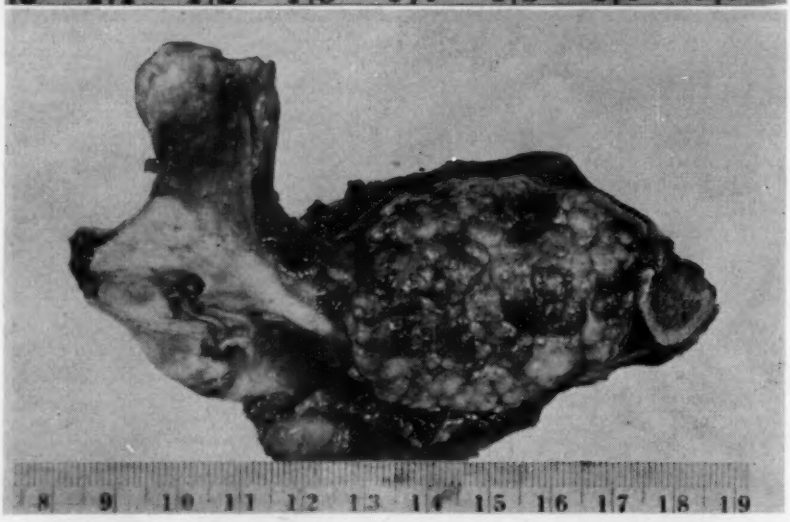


Fig. 6.—Photograph of gross specimen of verrucous carcinoma; note papillary character and associated leucoplakia.

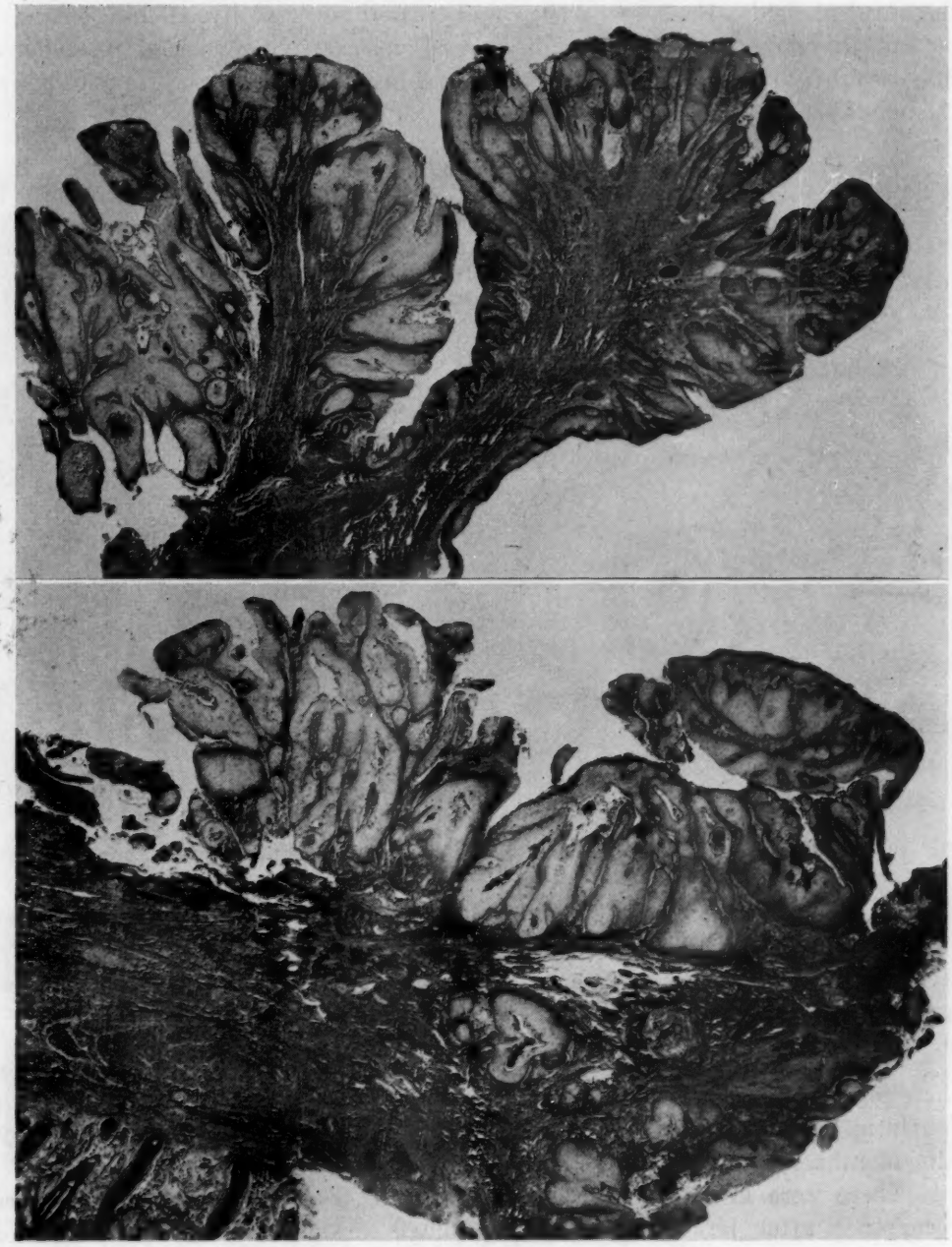
Fig. 7.—Photograph of gross specimen; typical pebbly verrucous carcinoma.

The biopsy material from this neoplasm is often confusing. Superficial biopies are often taken and a positive diagnosis of carcinoma cannot be made. Even with thin deep biopsies, which are recommended, diagnosis may be difficult because of the intact basement membrane and the well-differentiated nature of the growth. However, after the characteristic pathologic pattern is recognized,

even early lesions can be diagnosed and proper treatment instituted without delay.

These verrucous carcinomas of the oral cavity have been treated by a variety of methods:

Radiation Alone.—Seven patients were treated by radiation alone. In all of these, the lesion was rather superficial. Two died, both of pneumonia, one five months after therapy and the other eight months after. One patient had a



Figs. 8 and 9.—Frondlike, well-defined verrucous carcimona (very low power.)

recurrence after forty-two months, and the rest are living without disease after forty-one- forty-six, seventy-four, and eighty-six months, respectively, at the time of this communication.

Radiation Followed by Surgery.—In 7 instances, radiation was given and then recurrence necessitated surgery. Following irradiation, one patient had recurrence (outside the irradiated field) and then had surgery. This patient then developed five local recurrences (over a period of 2.5 years) just outside the surgical field. Each recurrence was treated successfully. Three of the 7 patients have died, but none of disease. Four are living without disease six, fifty-two, fifty-three, and sixty months. In 3 instances it was necessary to resect the mandible.

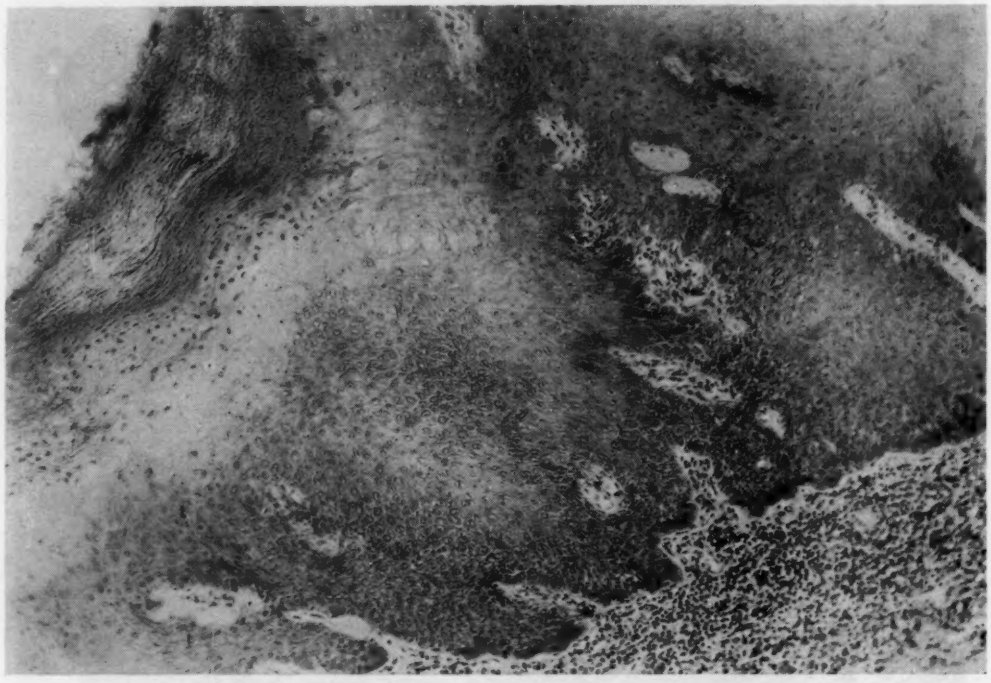


Fig. 10.—Point of transition between atrophic epithelium and beginning verrucous carcinoma (low power).

Local Excision.—Nine patients had local excision only; these patients are living four, six, nine, nine, twenty-six, thirty-one, and thirty-six months, respectively. One, at the end of twenty-four months, developed a local recurrence; another, at the end of eight months, died of intercurrent disease.

Excision Plus Mandibular Resection and Upper Neck Dissection.—One of these 8 patients died at eighteen months of intercurrent disease, but 7 are living fourteen, twenty-five, twenty-five, thirty-six, thirty-nine, forty-six, and forty-nine months, respectively.

There were 11 mandibular resections in all; 3 of these resections followed recurrence after irradiation. Roentgenologic examination revealed invasion every time that it was present (4 out of 11); when it was not present, because of

inflammatory attachment to periosteum together with pressure, there was marginal erosion. In only one instance was an erroneous diagnosis of invasion made. This was a patient in whom irradiation had been done previously, and

Fig. 11.—Actively growing edge of verrucous carcinoma, basement membrane is intact and inflammatory reaction is prominent (moderate enlargement).

Fig. 12.—Cystic changes and clublike fingers of well-defined epithelium (moderate enlargement).

the destructive changes in the mandible were a combination of radiation plus infection. In only one instance did a local recurrence appear after mandibular resection.

Radiation as a method of therapy is apparently successful in the relatively small, superficial lesions, but if the lesion has any size, then the chances of recurrence apparently increase, the recurrences often appearing just outside the irradiated field. In 14 patients treated by irradiation, 8 had recurrences. We have recently had two lesions too extensive for surgery, in which roentgen therapy gave excellent palliation. The cause for recurrence is unknown, but certainly there must be a predisposition of the epithelium over a wide area to become malignant. Inadequate local excision will also result in recurrence. One patient, for instance, had 5 recurrences, and there was local recurrence in 2 other instances after excision alone. If the lesion is extensive and is treated by irradiation, then it may recur, and surgery becomes somewhat more difficult. Of the group treated by primary mandibular resection, not one patient developed a local recurrence nor was there any operative mortality. Resection, therefore, seems to be the method of choice when the lesion is at all extensive. It is difficult to determine by roentgenologic examination how extensive the invasive process is, and more radical rather than conservative procedures are indicated.

SUMMARY

A type of squamous carcinoma of the oral cavity, designated as verrucous carcinoma, has been described. This lesion occurs predominantly in aged men, most commonly on the buccal mucosa and lower gingiva. Tobacco chewing may be of etiologic significance. Slowly growing, well differentiated, verrucous in character, and often extensive, this neoplasm tends to invade local structures (mandible, soft tissues, antrum). No distant metastases occurred in the group reported, and local metastases were rare. Local recurrence is common with inadequately treated patients. Radiation is successful in controlling small superficial lesions. For extensive lesions, radical surgery is indicated and often when fixation or invasion of bone is present, mandibular resection with upper neck dissection is justified.

A HIP NAIL COUNTERBORE

G. J. CURRY, M.D., FLINT, MICH.

(From the Section for Surgery of Trauma, Hurley Hospital)

SURGEONS selecting internal fixation for intertrochanteric femoral fractures frequently use the Smith-Petersen nail with a Thornton plate attachment. In many cases more comminution is found at operation than was disclosed by the x-ray film. This refers especially to the fracture lines occurring on the lateral surface. During the process of nail insertion, it has been the experience of many to find an advance in the comminution already present or the production of additional fracture lines. These accidents obviously cause variable degrees of interference with the security of nail fixation.

For the past two years I have used a counterbore (Fig. 1) with most satisfactory results. Its diameter corresponds to that of the Smith-Petersen nail, and enough of the femoral cortex is removed to produce a "set" for the nail. Inasmuch as the nail is inserted in a slanting projection, more of the

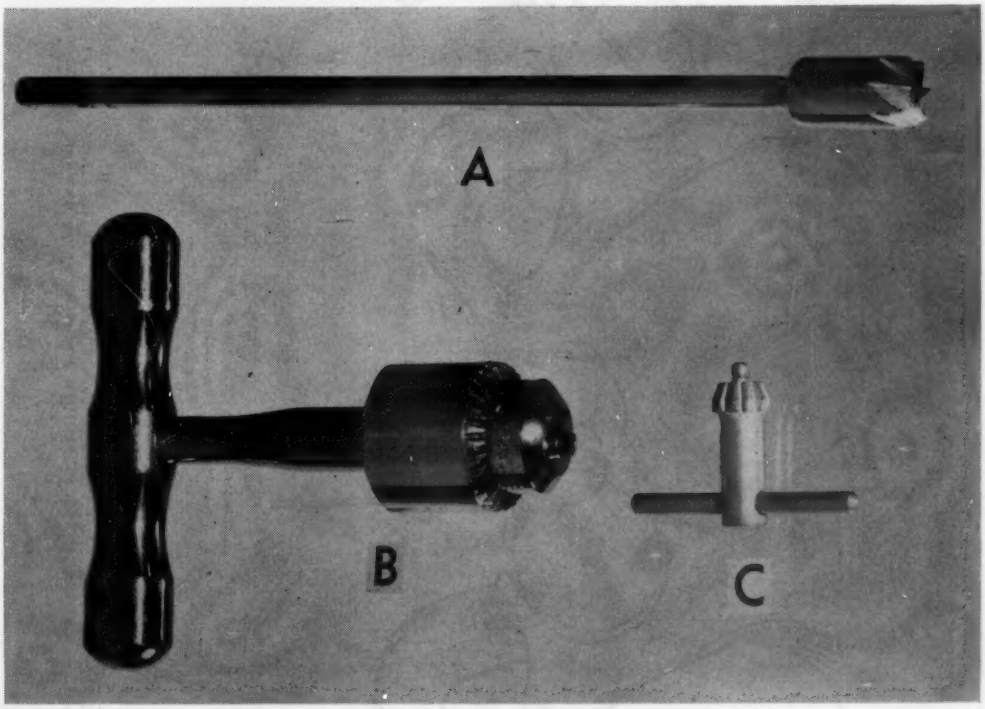


Fig. 1.—*A*, Photgraph of counterbore; *B*, handle; *C*, chuck used for fixation of the counterbore to the handle.

Received for publication, June 18, 1947.

Fig. 2.—Drawing of an intertrochanteric fracture with comminution and varus deformity.
Fig. 3.—Drawing showing depth of penetration by the counterbore which has been threaded over the guide pin.
Fig. 4.—Drawing showing fracture reduction and fixation by the use of a Smith-Petersen nail and Thornton plate.

cortex in the inferior portion should be removed. It is advised that complete penetration here be accomplished (Fig. 3). A partial removal superiorly will obviously follow. The head of the Smith-Petersen nail protrudes far enough to be attached to the Thornton plate.

The trial period covered its use in fifty cases. The constant finding was the elimination of additional trauma to the trochanteric cortex.

Erratum

On page 150 of the January, 1948, issue of the JOURNAL, in the article "The Problem of Parenteral Nitrogen Administration in Surgical Patients" by Arnold J. Kremen, one reference is incomplete. It should read: 123a. Clark, J. H., Nelson, W., Lyons, C., Mayerson, H. S., and DeCamp, P.: Chronic Shock: The Problem of Reduced Blood Volume in the Chronically Ill Patient (in three parts), Ann. Surg. **125**: 218-247, 1947.

Case Reports

AN UNUSUALLY LARGE MYXOSARCOMATOUS TUMOR OF THE SUBMAXILLARY GLAND

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(From the Department of Surgery, University of Utah Medical School and Latter Day Saints Hospital)

IT IS most unusual, in these days of modern medicine, to encounter such a large deforming neoplasm of the face as the one characterized in the accompanying photographs (Fig. 1). Forty-six years were required for this pathologic curiosity to develop. During this period the patient consulted many physicians but it was their conflicting advice as to the therapeutic management which resulted in her bewildering procrastination. Why should there be so much confusion in the minds of the men of our profession as to the correct method of handling these tantalizing tumors? Surely this case demonstrates the fact that even benign neoplasms of the submaxillary gland can and do undergo malignant transition if they are given sufficient time in which to make the change.

CASE REPORT

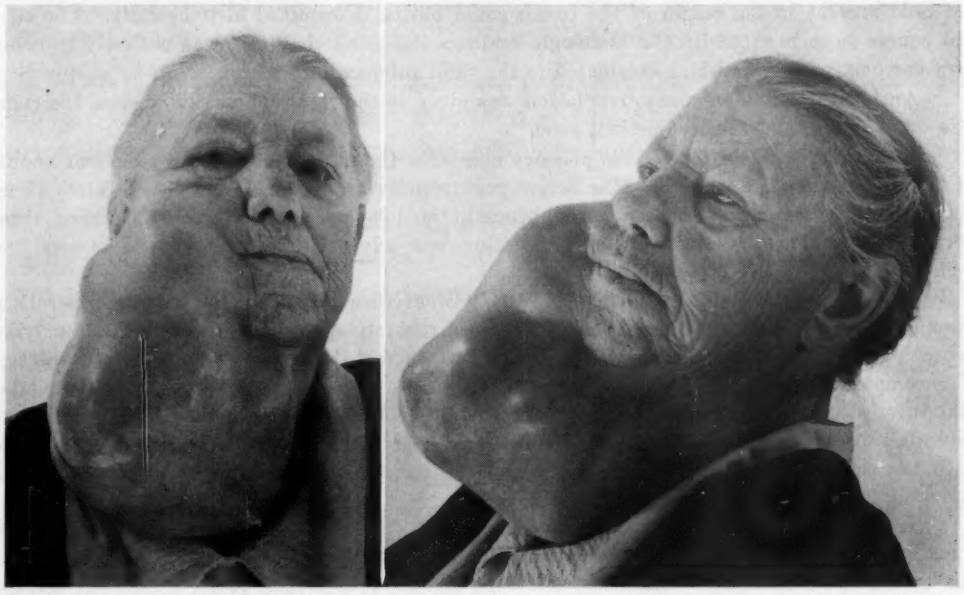
Mrs. C. B., a 66-year-old housewife of Bohemian birth, was admitted to the Latter Day Saints Hospital, on Sept. 18, 1942, because of a "lump in the neck." She insisted that the tumor first appeared forty-six years previously, in the region of the right submaxillary gland. At that time she was told by a physician that the "lump" represented a swollen lymph gland originating from an ulcerated tooth. The mass had persisted, however, even after the offending tooth was removed. Seven years before admission, when the patient was 58 years of age, the "lump began to grow," particularly during the eighteen months prior to admission.

Interestingly, the presenting complaints were all related to the size, weight, and position of the tumor. She was constantly annoyed by the dull aching pain along the right side of the head and face, which could be effectively relieved by manually supporting the weight of the tumor. When working, she wore a scarf, which passed in a hammock-like fashion beneath the tumor and was tied on top of the head to sustain the weight of the mass. Her concern was that the "lump is so big that it is always getting in my way." One day she snagged the lower pole of the pendulous tumor on the hook of a screen door, producing such a deep laceration that an alarming hemorrhage resulted. On another occasion she was putting wood in the stove and the protruding mass came in contact with the stove, thereby producing an extensive third degree burn. Deglutition was becoming painful and difficult, and pressure on the trachea caused considerable respiratory embarrassment. She was compelled to sleep on the right side in such a position that the entire weight of the tumor could be supported by an extra pillow. She insisted that she had never had a sick day in her life and could do more work than most young women.

Received for publication, July 14, 1947.

During the past five years she had consulted many different physicians and they all advised her to "leave this cancerous growth alone as you will die if anyone attempts to remove it." So persuasive were these arguments that her own son, a very competent physician, and her two daughters, both of whom are registered nurses, could not persuade their mother to submit to surgery. The only reason she finally consented to have an operation was because the neoplastic mass began to undergo discoloration and she thought it was "abscessed."

The only abnormal findings on physical examination were related to the football-sized tumor which occupied the entire right cervicofacial area. Its exact size and location can best be ascertained by consulting the accompanying photographs (Fig. 1). The pendulous tumor was bosselated, firm, and not tender. It was so intimately attached to the deep structures of the neck that any attempt to manipulate the neoplasm resulted in a compressive occlusion of the trachea. The overlying skin was taut, thin, and had a peculiar bluish discoloration as if covering a huge hemangioma. No portion of the right parotid could be identified because the mass completely covered this area. The facial nerve, however, was still functioning. The



A. *B.*

Fig. 1.—*A*, Front view of a patient with a myxosarcomatous tumor arising in the right submaxillary gland. The excised tumor weighed 2,450 Gm. *B*, Lateral view of the same patient.

expanding tumor had pushed the floor of the mouth upward so that the tongue was resting against the hard palate. The mucous membrane of the oral cavity was intact. The left submaxillary and sublingual glands appeared to be normal. Endoscopic studies demonstrated a rotation and compression of the trachea but without evidence of actual infiltration. The vocal cords exhibited their normal range of motion. X-ray studies of the lungs, skull, the vertebrae failed to show metastatic invasion. On the presumptive diagnosis of a "mixed tumor of the right submaxillary gland," surgical intervention was advised.

At operation, because of the pronounced compression and distortion of the trachea, it was felt that cyclopropane should be administered by the endotracheal method. The tumor mass was exposed by a transverse skin incision. It was surprising to see the ease with which the encapsulated tumor was separated from the parotid gland and other cervicofacial structures. The tumor had not invaded the trachea but merely compressed it. When the dissection had been carried down to the right submaxillary fossa it was found that the neoplasm had invaded fascial planes along the floor of the mouth. Neoplastic extensions had invested the sheath and outer coatings of the carotid vessels. In spite of this widespread dissemination an extensive block dissection of the right side of the neck was carried out. Care was taken

not to enter the oral cavity, therefore, Wharton's duct was ligated and divided near its mucosal orifice. Closure was accomplished with ease and the patient made a pleasing recovery.

The excised tumor measured 19.5 by 20 by 18 cm. and weighed 2450 Gm. The skin was smooth and freely movable over the tumorous mass and in several small areas it presented a bluish discoloration suggestive of underlying hemorrhage. The remaining two-thirds of the tumor was covered by a well-defined but lobulated capsule. Sections through the neoplasm revealed a yellowish white, soft or gelatinoid tissue with scattered areas of hemorrhage and necrosis. The tissue presented a relatively uniform appearance throughout.

Microscopically the tumor possessed an extremely loose, myxomatous stroma, containing stellate or spindle cells. The cellularity varied throughout the sections; in some areas, the tumor was quite acellular, and in others numerous cells were seen. In the cellular zones the mitotic figures were numerous and the cells radiated out from the vessels, producing a peritheliomatous appearance. The excessive vascularity of the tumor was due to the presence of numerous, large, dilated venous sinuses. Deposits of degenerating blood pigments within the cells evidenced previous hemorrhagic episodes. There were no gland structures or epithelial cells present so the origin of the tumor could not be determined histologically. The clinical course supplemented by the histologic findings indicated that this was a slowly growing myxosarcomatous tumor which originated in the right submaxillary gland.

An intense course of x-ray irradiation was given to the right submaxillary area, the right side of the neck, and the mediastinal zone.

About eleven months after the primary operation the patient observed a recurrent nodule in the right submaxillary area. The tumor grew rapidly but produced no discomfort. Three months later a second nodule appeared beneath the lobe of the right ear. Both of these neoplasms grew rapidly and further irradiation was advised against until the tumors had been excised.

The second admission was Nov. 10, 1944, twenty-five months after the first operation, when she was readmitted for excision of the recurrent nodules. The lemon-sized mass lying beneath the lobe of the right ear was easily excised, in fact, it seemed to be well encapsulated. The companion tumor in the right submaxillary fossa, however, had completely surrounded and invaded the larynx, trachea, and the carotid vessels. Technically it was impossible to excise all of the spreading neoplasm, therefore, only the main mass of the tumor was removed with the cautery. The wound was closed and the patient was discharged from the hospital one week later.

It was reported that the specimens consisted of four pieces of tissue varying from 4 to 6 cm. in length. These fragments were irregular in size and shape and presented a homogeneous gelatinous consistency. Microscopically the stroma presented a loose, edematous stroma. The basic cell was rather fat, plump, and hyperchromatic. Mitosis was rather frequent, much more so than in the specimen which had been removed twenty-five months previously. The morphology and clinical course was consistent with diagnosis of a recurrent myxosarcomatous tumor of the right submaxillary gland.

The residual tumorous tissue continued to grow and additional x-ray therapy was given to the right pre-auricular area and to the right submental zone.

In spite of the additional irritation the tumor grew rapidly. It invaded the floor of the mouth, pushing the tongue so firmly against the hard palate, that both speech and deglutition became impossible. Direct infiltration of the trachea so obstructed the air passage that breathing was most laborious. Complete motor and sensory paralysis of the lower extremities occurred when the neoplastic process destroyed the second and third lumbar vertebrae, thereby exerting pressure on the spinal cord. Nausea and vomiting, associated with a persistent headache, announced the presence of cerebral metastasis. This impression was further confirmed by the development of a bilateral optic atrophy associated with paralysis of the external ocular muscles, all secondary to direct metastasis to the brain and the concomitant increase in intracranial pressure. She died, forty-nine months after the primary operation. Autopsy studies were not made because the patient died in a small town where such facilities were unavailable. The clinical course, however, left no doubt that death was due to a generalized metastasis of the malignant tumor which had its origin in the right submaxillary gland.

DISCUSSION

If one reads the voluminous literature which has been published during the past thirty years on the subject of "mixed tumors of the salivary glands," he emerges from such a study in a state of abject confusion. Pathologists cannot agree on the origin, the histologic classification, or even the course these perplexing tumors will follow. For example, Hertzler,[4] in his excellent monograph on *Tumors of the Neck*, stated, "I have yet to see a tumor of the submaxillary or sublingual salivary glands invade the surrounding tissues or recur after its removal." This leads one to believe that these mixed tumors are relatively benign. On the other hand, Blair, Moore, and Byar[1] reported eight neoplasms of the submaxillary glands of which 50 per cent were definitely malignant. Wood[7] and Ewing[3] both maintained that these mixed tumors are potentially malignant, undergoing both carcinomatous and sarcomatous transitions.

The management of these tantalizing tumors likewise presents conflicting views. Hertzler insisted that "these mixed tumors of the submaxillary gland are well encapsulated, therefore, they can be removed safely by enucleation without sacrificing the submaxillary gland itself." Patey[6] believed it to be unwise to leave the submaxillary gland behind even though the mixed tumor can be easily enucleated. He pointed out that these tumors have a multicentric origin and that many of the so-called recurrences do not represent a recurrence of the excised tumor but a similar growth arising in part of the gland that was not disturbed by the primary operation. He, therefore, felt it wise to remove the submaxillary gland and its invested neoplasm, even though the tumor presents clinical and histologic evidence of benignancy.

After studying eighty-one cases of primary and recurrent malignancies of the submaxillary glands, Dockerty and Mayo[2] condemned all forms of conservative therapy. In dealing with a "mixed tumor," they insisted that the parent submaxillary gland and the tumor should be removed en masse. If an immediate examination of the excised tissues confirms the diagnosis of benignancy then nothing further need be done. If, however, the tumor mass shows evidence of malignancy, specimen of regional tissues are removed and given to the pathologist. If histologic studies indicate that the neoplastic process has spread beyond the confines of the submaxillary gland they believe that a radical unilateral dissection of the neck should be done. Likewise, if the primary submaxillary tumor is anaplastic, even though there is no evidence of local invasion they resort to a radical block dissection of the neck. We agree with this concept.

Unfortunately many "mixed tumors" have spread to important regional structures before the patients submit to surgery.[5] Technically, it is impossible to excise the infiltrative process once it has invaded the trachea, hypopharynx, or carotid sheath. In such instances one can excise the main mass of neoplastic tissue and then rely on the inhibitive influences of irradiation to further delay the inevitable extension. While irradiation is seldom curative it often retards the growth of the infiltrative process.[5]

SUMMARY

Mixed tumors of the submaxillary gland may originate as benign tumors but they most certainly possess potentialities of malignant transition. In our case it required forty-six years for the evolution of this malignant change. Histologically the excised tumor represented areas of "mixed tumor formation," and in others there were anaplastic zones showing definite myxosarcomatous changes. During the first fifty-five years of its development the tumor presented all the signs of being a benign growth, but during the last two years it exhibited clinical characteristics of malignancy. Rapid growth, recurrence after excision, and metastasis to the brain, lungs, vertebrae, and skull, combined with infiltration of the trachea, carotid sheath, hypopharyngeal structures, and the gland on the opposite side of the neck most certainly stamped the tumor as being malignant.

Conservatism, such as simple enucleation of a benign mixed tumor of the submaxillary gland, is to be condemned. The submaxillary gland and the growing neoplasm should be removed en masse. If histologic studies of the excised specimen demonstrate malignant changes, then a block dissection of the neck is indicated. This is particularly true if the neoplastic process has spread beyond the confines of the capsule of the submaxillary gland. Experience dictates that such a plan greatly minimizes the incidence of recurrence.

REFERENCES

1. Blair, V. P.: Moore, S., and Byar, L. T.: Cancer of the Face and Mouth, St. Louis, 1941, The C. V. Mosby Company.
2. Dockerty, M. B., and Mayo, C. W.: Primary Tumors of the Submaxillary Gland With Special Reference to Mixed Tumors, Surg., Gynec. & Obst. **74**: 1033-1045, 1942.
3. Ewing, J.: Neoplastic Diseases: A Treatise on Tumors, ed. 4, Philadelphia, 1940, W. B. Saunders Company.
4. Hertzler, A. E.: Surgical Pathology of the Diseases of the Neck, Philadelphia, 1937, J. B. Lippincott Company.
5. McFarland, J.: Mixed Tumors of the Salivary Glands, Surg., Gynec. & Obst. **63**: 457-468, 1936.
6. Patey, D. H.: The Mixed Tumors of the Salivary Glands, Brit. J. Surg. **18**: 241-258, 1930.
7. Wood, F. C.: Mixed Tumors of the Salivary Glands, Ann. Surg. **39**: 57-67, 1930.

Recent Advances in Surgery

Conducted by Alfred Blalock, M.D.

INTRAVENOUS CLOTTING

An Analysis of Five Hundred Cases Observed in Army Personnel at the Vascular Centers

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DURING their period of operation, 502 instances of intravenous clotting were observed in Army personnel at the vascular centers at DeWitt General Hospital, Ashford General Hospital, and Mayo General Hospital. These figures, however, cannot be assumed to be representative of the incidence of this condition in the entire United States Army. All patients with intravascular clotting were not treated at the vascular centers, which received only complicated cases, recurrent cases, and cases in which ordinary methods of therapy did not achieve results. The assessment of these cases as an over-all picture of intravascular clotting within these limitations is valid, but conclusions must be drawn with due regard to the background.

Care was taken to exclude from the series all cases of thrombophlebitis migrans, which presents a special problem in relation to Buerger's disease and which should, of course, be considered as a possibility in any case of superficial thrombophlebitis.

Intravenous clotting falls into two categories, thrombophlebitis and phlebothrombosis. Thrombophlebitis, because it is an inflammatory process, gives rise to more or less severe reactions, but is usually simple to diagnose and is seldom complicated by pulmonary embolism. Phlebothrombosis, because it is a bland, quiet, non-inflammatory process, gives rise to few or no symptoms in the early stages, is frequently difficult to detect, is not infrequently followed by pulmonary embolism, and therefore is a potentially fatal lesion. The importance of differentiating between the two types of intravascular clotting has been repeatedly emphasized by Ochsner and DeBakey.[145, 147-149]

Not all instances of phlebothrombosis result in pulmonary embolism, nor do all pulmonary embolisms terminate fatally, but that the danger is real is indicated by both the reported incidence and the case fatality rate. The reported necropsy incidence of embolism varies from 1 per cent to almost 12 per cent[18, 50, 55, 84, 85, 116, 181] and the reported case fatality rate from 2.5 to 5 per cent.[84, 85, 116] The risk, furthermore, is not limited to either medical or surgical conditions. The report by Hunter and his associates[84] of eleven deaths from pulmonary embolism in 200 necropsied cases, is typical in its distribution: Five deaths occurred in medical and six in surgical cases.

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The incidence, the potential death rate, and the disabling end results of intravenous clotting thus make it a problem of serious concern to both physicians and surgeons in its immediate and its future implications. That statement is as applicable to military medicine as it is to civilian medicine.

INCIDENCE

Sex and Race.—Four hundred ninety-six of the 502 patients with intravenous clotting observed at the vascular centers in the Zone of the Interior during World War II (98.8 per cent) were white. This is a disproportionately high incidence, although the nonwhite elements of the United States Army at no time numbered more than 12 per cent.

From the standpoint of sex the figures are heavily weighted. The 27 women in the 502 cases (5.4 per cent) were nurses and WACs.

Reports in the literature are not in complete agreement as to the sex incidence of intravascular clotting. Matas[115] in a study based on reports from leading American and European clinics, found the incidence after operation practically the same for both sexes, as did Hunter and his associates[85] in 351 cases of deep venous thrombosis. Allen and his associates[2] and Fine and co-workers[66] reported a much higher incidence in men, and Veal and Hussey,[192] in a personal series of 84 cases, reported that 55 cases occurred in men against 29 in women, a disproportion which perhaps can be explained by the fact that most of their cases represented propagating thromboses requiring surgical treatment. Barker and his associates[13] reported that in acute thrombophlebitis as observed at the Mayo Clinic the ratio of women to men was 3:2. Both thrombosis and embolism were relatively more frequent in women, but fatal embolism was more frequent in men. McCartney's[116] figures suggest a somewhat opposite trend. In 689 cases of intravascular clotting which occurred in 25,771 necropsies, the incidence in men was 9.1 per cent and in women 11.2 per cent, while the proportion of fatal embolisms was 2.2 and 3.3 per cent, respectively. Post-partal cases are not included in the calculations.

Age.—From the standpoint of age the figures are also heavily weighted, most of the patients being between the ages of 20 and 39 years, because that age group included the great majority of all military personnel. In the 189 cases of intravascular clotting observed at DeWitt General Hospital, for instance, 54.6 per cent of the patients were between 20 and 29 years of age, and 41.1 per cent between 40 and 49 years. The average age was 26.8 years, although the age range for the whole series was 19 to 59 years.

Although the figures are weighted, the relative youth of the patients in this series of cases is worthy of comment, since thrombosis and embolism are generally regarded as complications of advancing age. Any type of peripheral venous thrombosis is most unusual in the first two decades of life, and all available statistics show the greatest frequency, as well as an increasing frequency, over 40 years of age.[34, 53]

McCartney,[116] for instance, in 25,771 necropsies, found the incidence of thromboembolism highest in the sixth and seventh decades. Eighty-one per cent of the patients in Stich's[184] series were over 40 years of age, 66 per cent over

60 years, and 20 per cent over 70 years. Fifty per cent of Miller and Rogers'[121] patients were over 50 years of age. Seventy per cent of Veal and Hussey's[192] 84 patients with deep venous thrombosis of the lower extremity were over 40 years of age, and more than 80 per cent of Allen, Linton, and Donaldson's[2] 367 patients were in this age group. Culp,[38] in a study of 38 instances of embolism in 4,070 deaths after operation, found that 62.5 per cent were in persons over 60 years of age, although only 41.2 per cent of all patients in the series were in this age group.

The age incidence is naturally related to other factors. Ewald,[65] the average age of whose patients was 26.8 years, stated that intravenous clotting occurred in young persons only in the presence of circulatory disturbances. Since slowing of the blood stream has been established as an important cause of intravascular clotting, it would be expected that the incidence would increase with age, since the circulation time slows with age. Koch[91] reported the circulation time to average 18 seconds between the ages of 15 and 19 years, 21 seconds between the ages of 30 and 40 years, and 23 seconds at 70 years. He also reported that it was longer at all ages after operation and in patients with circulatory disturbances. These considerations are not applicable to any of the 502 patients in the Army series, although indirect proof of their validity is found in the impressive reduction in the incidence of thrombosis and embolism achieved whenever preoperative measures to prevent and correct circulatory disturbances[69, 93, 174, 187, 197] are instituted.

PREDISPOSING AND PRECIPITATING FACTORS

Predisposing and precipitating factors are charted in Fig. 1. Though the fact is frequently overlooked, a large number of cases of intravascular clotting occur in the absence of any obvious causes. The proportion of spontaneous cases in the Army series was 27.1 per cent, and in 20 of the 84 cases reported by Veal and Hussey[192] there was no apparent cause; in 4 of their 20 cases the thrombosis originated in superficial varicosities and extended to the deep venous system. A detailed discussion of this group of cases would not be profitable, since it would entail analyses of individual cases from the standpoint of posture, hydration, varicosities, smoking habits, obesity, foci of infection, anemia and other blood dyscrasias, and similar considerations.[146] It must be emphasized that intravascular thrombosis is not only a surgical but a medical problem as well.[26]

In addition to the 136 cases of apparently spontaneous origin in the 502 cases of intravascular clotting which make up the Army series, the vascular lesion may be classified as traumatic in 183 cases (36.5 per cent), postoperative in 71 (14.1 per cent), and associated with previous illness in 92 (18.3 per cent). In the remaining 20 cases (4.0 per cent) miscellaneous causes seemed responsible.

Direct trauma to the blood vessels, such as may occur in fractures, sprains, and gunshot and stab wounds, is an obvious cause of intravascular clotting. Injuries of this kind are often associated with tearing, stretching, or crushing of regional vessels, and in other instances, though the vessel itself may not be

directly implicated, the thrombus may originate at the site of injury and propagate itself from there. In the Army series, 109 of the 183 cases of traumatic origin (Fig. 2) followed local injury, chiefly direct contusions and lacerations of the tissues of the extremities, and 10 followed fractures. That fractures frequently predispose to intravascular clotting is shown in numerous reports from the literature. In 12 of the 15 instances of pulmonary embolism following trauma reported by McCartney[117] in a total of 73 cases of pulmonary embolism the patients had sustained fractures of the lower extremities and were confined to bed, and Potts,[162] who reported 5 cases of thrombophlebitis in 95 fractures of the lower extremity, considered the complication at least partially due to immobilization.

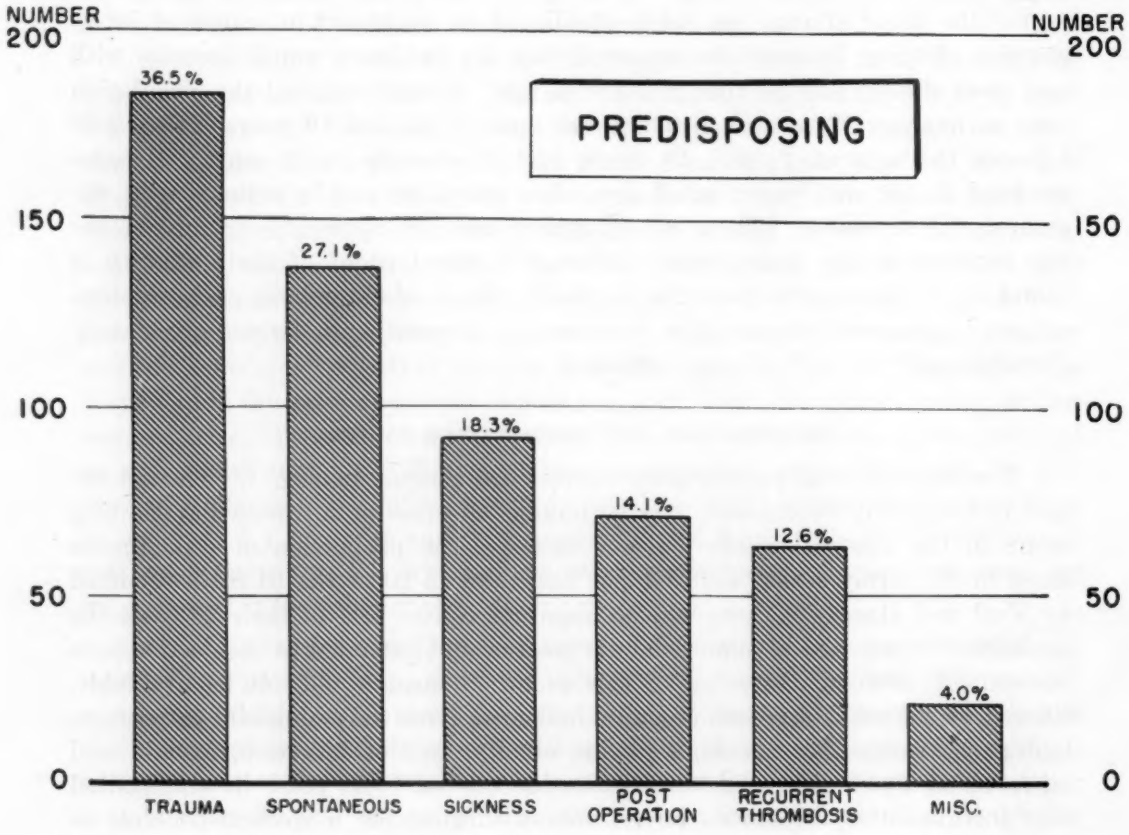

Fig. 1.

Ochsner and DeBakey,[150] who emphasized trauma as an important factor in intravascular clotting, also attempted to explain why clotting does not occur more frequently following extensive injury to an extremity. Trauma of equal severity elsewhere in the body, they pointed out, would produce blood changes (increased viscosity, hyperglobulinemia, hyperproteinemia, increased fibrinogen, antitryptic power, peptidase and calcium and decreased carbon dioxide combining power of the plasma),[148] sufficient to be considered as factors in the production of thrombosis. Other changes under these circumstances, including an increase in the formed elements of the blood and increased coagulability,[148, 208, 209]

would also favor the production of thrombosis. The immobilization of an extremity in a cast would therefore seem to produce an ideal situation for the development of intravascular clotting. The lesion does not develop more frequently, according to Ochsner and DeBakey,[148] for two reasons, the youth of the patients who most frequently sustain fractures, and the vasodilating effect of choline and the increased heat of the part. It is quite possible that intravenous thrombosis subsequent to trauma is the result of injury to the vascular endothelium, with resultant acute thrombophlebitis, as distinguished from phlebothrombosis, in which the manifestations and mechanism of production are quite different.

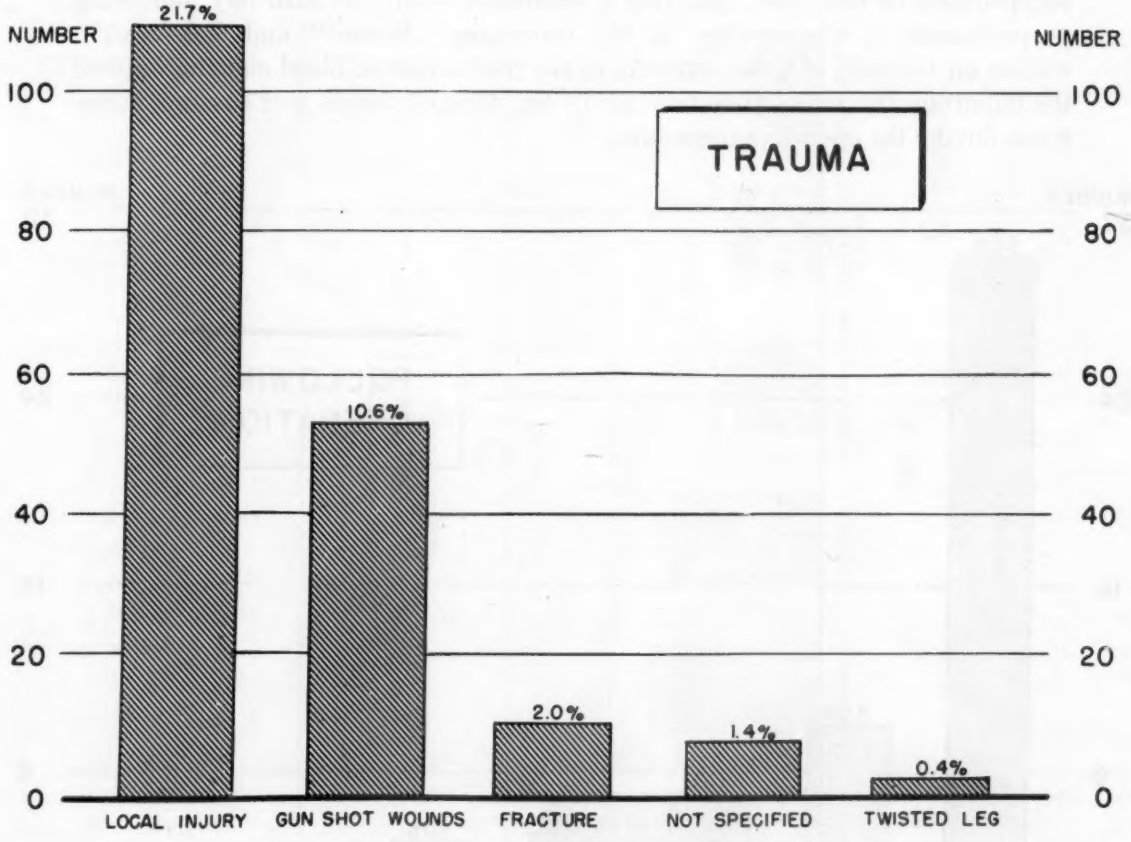

Fig. 2.

The importance of operative trauma (Fig. 3) in the production of intravenous clotting is supported by many observations.[21, 59, 61, 62, 71, 93, 107, 134] In the 71 cases in this category in the Army series the lesion followed appendectomy in 30 and hernioplasty in 10, but the figures are not particularly significant, since these are the two most frequent noncombat-connected operations performed in military hospitals.

Of the numerous reasons why the postoperative state predisposes to intravenous clotting, three are most important: (1) slowing of the blood stream, which is most marked in prolonged operations and which is associated with

diminished cardiac action and lowered blood pressure; (2) injury of the endothelium; and (3) changes in the composition of the blood. Changes in the composition of the blood affect the prothrombin time, clotting time, calcium time, sedimentation rate, and platelet count. The blood platelet count rises on the fourth day after operation, reaches a maximum on the twelfth day, and does not revert to normal until the twenty-first day. According to Wright[208, 209] the platelets also become sticky, their adhesiveness increasing as they increase in numbers; the change is in the thrombocytes rather than in the serum. Newburger,[139] on the other hand, has pointed out that thrombosis may occur before the fourth postoperative day. Lambret and Driessens[100] reported a postoperative rise in polypeptides of the blood, reaching a maximum about the fifth day and being proportionate to the severity of the procedure. Mason[114] and Takaura's[188] studies on the part of tissue extracts in the production of blood clotting implied the importance of sharp dissection, gentle handling of tissues, and absolute hemostasis during the operative procedure.

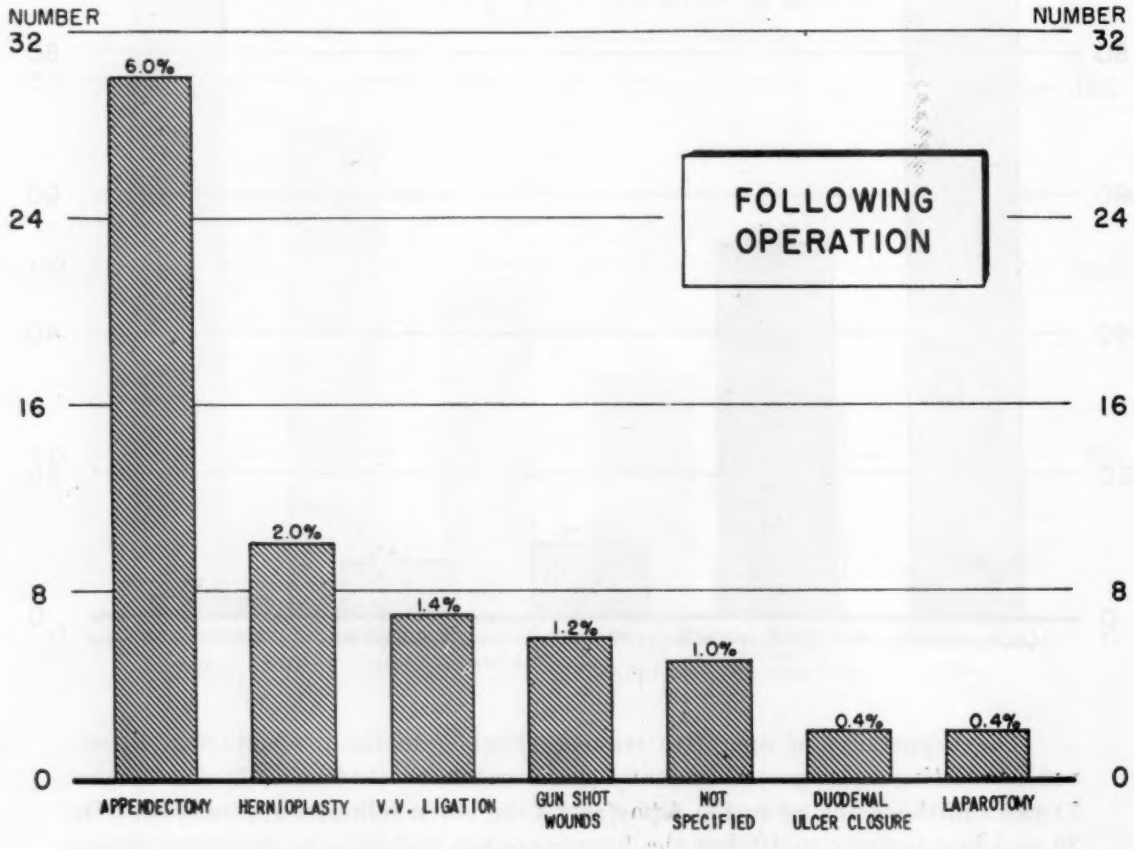

Fig. 3.

Of the various types of illness (see Fig. 4) which preceded 92 cases of intravenous clotting in the Army series, pneumonia accounted for 24 cases. Others, including myself,[90] have emphasized the importance of pneumonia as a predecessor of pulmonary embolism. White[206] has emphasized another important point, that the increasing accuracy in the diagnosis of pulmonary emboli has

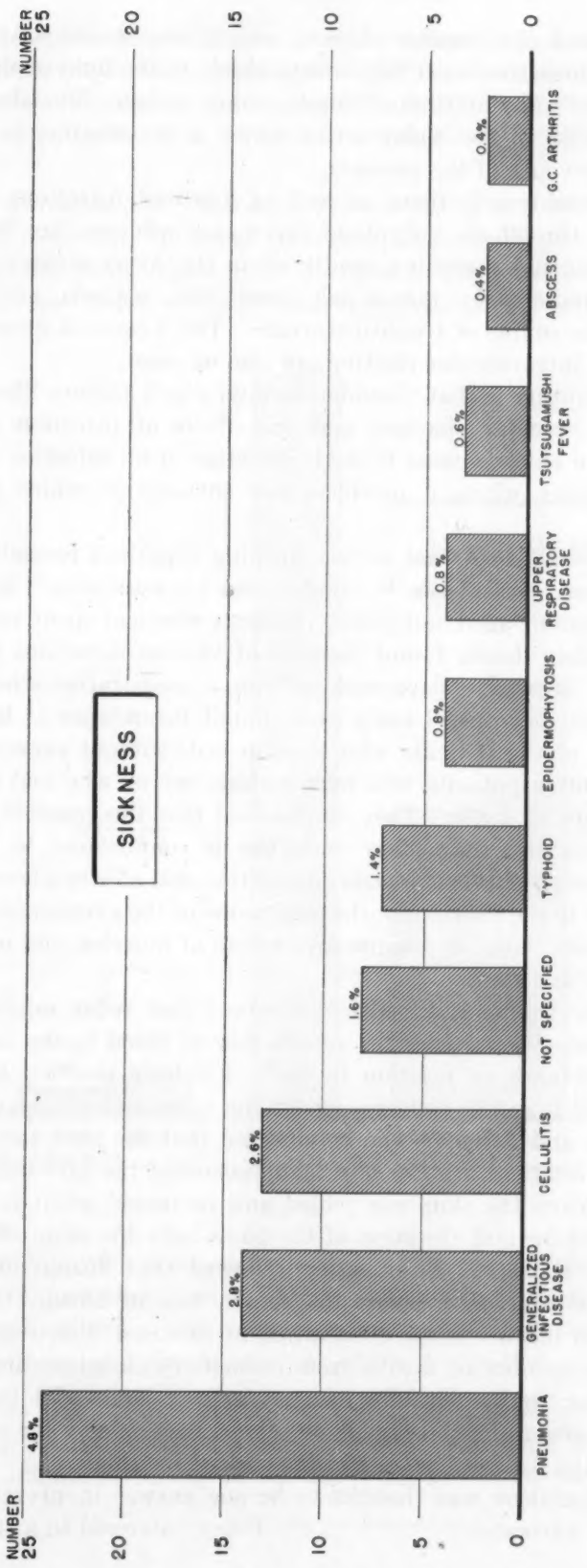
NUMBER
25
20
15
10
5
0
SICKNESS
4.8%
2.8%
2.6%
1.6%
1.4%
0.8%
0.8%
0.6%
0.4%
0.4%
PNEUMONIA
GENERALIZED INFECTIOUS DISEASE
CELLULITIS
NOT SPECIFIED
TYPHOID
EPIDERMOPHYTOSIS
UPPER RESPIRATORY DISEASE
TSUTSUGAMUSHI FEVER
ABSCESS
G.C. ARTHRITIS

Fig. 4.

materially reduced the number of cases which once would have been listed as pneumonia or congestive heart failure but which, in the light of the newer knowledge, are now correctly attributed to pulmonary emboli. The absence of preceding cardiac disease in the Army series, which is noteworthy, is probably to be attributed to the youth of the patients.

Certain systemic infections, as well as localized infections, are frequently associated with thrombosis. Typhoid fever and influenza are important examples. Rather unusual preceding conditions in the Army series include tsutsugamushi fever, jungle ulcer, poison oak, insect bite, malaria, and other illnesses contracted in the course of tropical warfare. The 2 cases of gonorrheal arthritis which preceded intravascular clotting are also unusual.

The presumption is that thrombophlebitis which follows illness is caused by blood changes, vascular changes, and the effects of infection and circulatory retardation. An obvious cause is the localization of an infection in the intima of a peripheral vessel, where it produces raw surfaces on which platelets can be deposited.

It is well established that merely keeping a patient recumbent in bed predisposes to venous thrombosis.[54] Hunter and his associates,[85] in 351 necropsies performed on middle-aged and elderly patients who had spent various periods of time in bed before death, found thrombi of various durations present in more than one-half. Hunter and co-workers,[84] in a comparative study of two series consisting of 200 necropsied cases each, found thromboses of leg veins present in 59 per cent of the patients who were in bed, without exercise, as compared with 44 per cent in patients who were ambulatory or who had exercised within forty-eight hours of death. They emphasized that the common denominator of phlebothrombosis and pulmonary embolism is confinement to bed because recumbency favors mechanical venous obstruction and affects adversely the efficient return of blood to the heart from the deep veins of the extremities, which depends on the circulation time, the compressive action of muscles, and negative pressure in the abdomen and thorax.

Luckhardt, Alpert, and Smith[110] observed that reflex inhibition of respiration will temporarily obstruct the return flow of blood to the heart and emphasized the importance of position in bed. Fowler's position is generally condemned because it causes compression of the veins and retardation of the blood flow.[178] Smith and Allen,[180] who emphasized that the most important influence on the circulation time was the skin temperature of the extremities (the velocity being slowed when the skin was cooled and increased when it was warm), observed that exercise and elevation of the parts have the same effect on the circulation time as warmth. Friedlander[77] showed that flexion of the thigh with elevation of the extremity favors the return flow of blood. Of importance in connection with posture is the observation of Simpson[178] concerning the striking increase in the number of deaths from pulmonary embolism among elderly persons who during the London blitz had sat for long hours with the legs dependent and with the pressure of the edge of the chair, particularly the crossbar of a deck chair, against the popliteal space and the back of the thigh.

Early ambulation was thought to be one answer in preventing thrombosis and has many advocates.[32, 170, 180, 197, 212] Coley[35] stressed in a study of operative

cases in 30 hospitals in the 8th Service Command that no patient allowed up out of bed within seventy-two hours had detectable intravenous clotting or embolism. In any event early activity in bed is desirable.[23, 160, 169, 170, 195, 207] The significance of such exercise has been repeatedly emphasized.[14, 21, 119, 145, 147-149, 161-163, 176, 186, 201, 205]

Recurrent Intravascular Clotting.—Sixty-three of the 502 patients in the Army series (12.6 per cent) had had previous episodes of thrombophlebitis. This is a consideration of great importance. No cases in this series were fatal, but the advice of Barker and his associates[13] concerning the careful management before

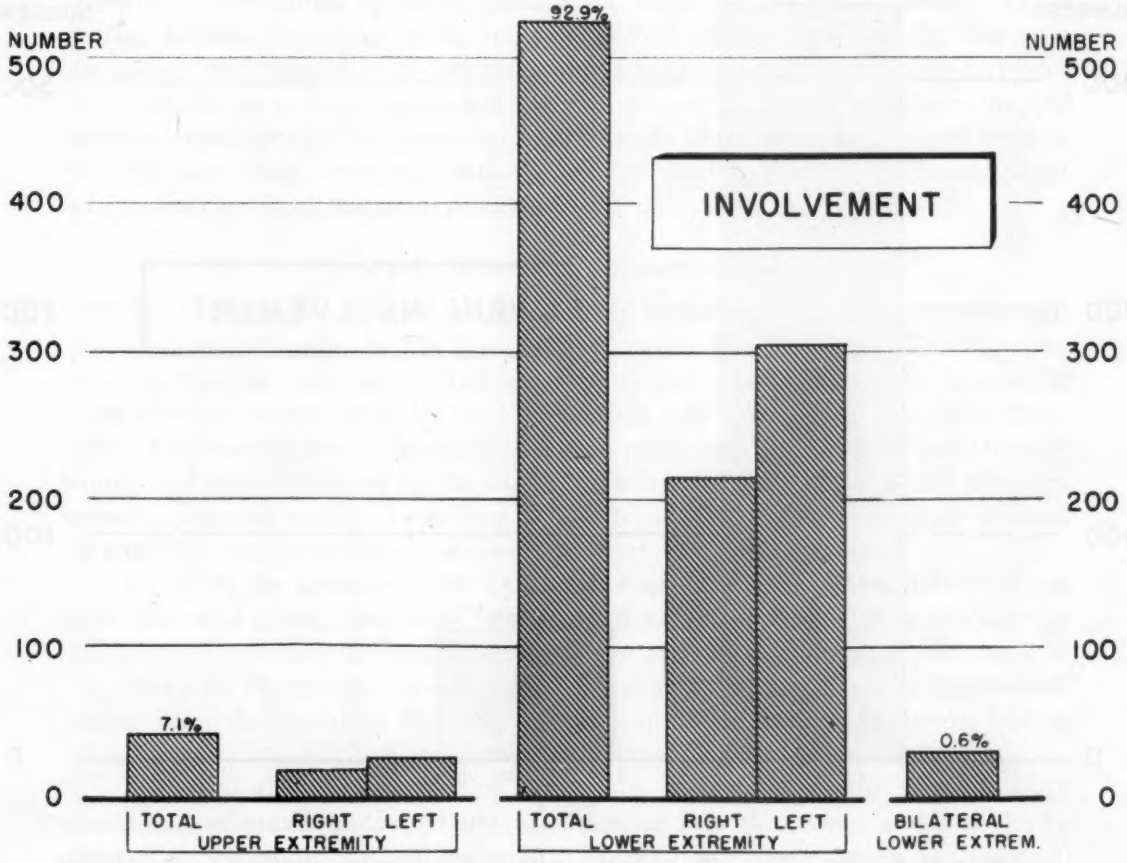

Fig. 5.

operation of patients with residual findings of previous thrombophlebitis is emphasized by the figures they report: Of 46 patients in their series who gave a history of thrombophlebitis less than one year before operation, 31 developed pulmonary embolisms, and almost one-half of the group died.

Miscellaneous Causes.—In the 20 cases of intravascular clotting of miscellaneous origin in the Army series, 7 were associated with some form of strenuous effort, such as hiking, carrying packs, throwing baseballs, and other athletic endeavors.

The remaining 13 cases were associated with varicose veins, which in one instance had been injected. The importance of this cause of intravascular clotting has been repeatedly stressed.[11, 65, 68, 146, 163, 192] The existence of varicosities favors venous stasis, which is an important factor in thrombosis. For this reason, varicosities must be corrected preoperatively or treated by compression bandages during the operative and postoperative period. Compression bandages have been shown to be effective postoperatively in reducing the incidence of thrombophlebitis even in the absence of varicosities.[68] The thrombosis usually begins in the superficial veins and extends to the deeper veins.

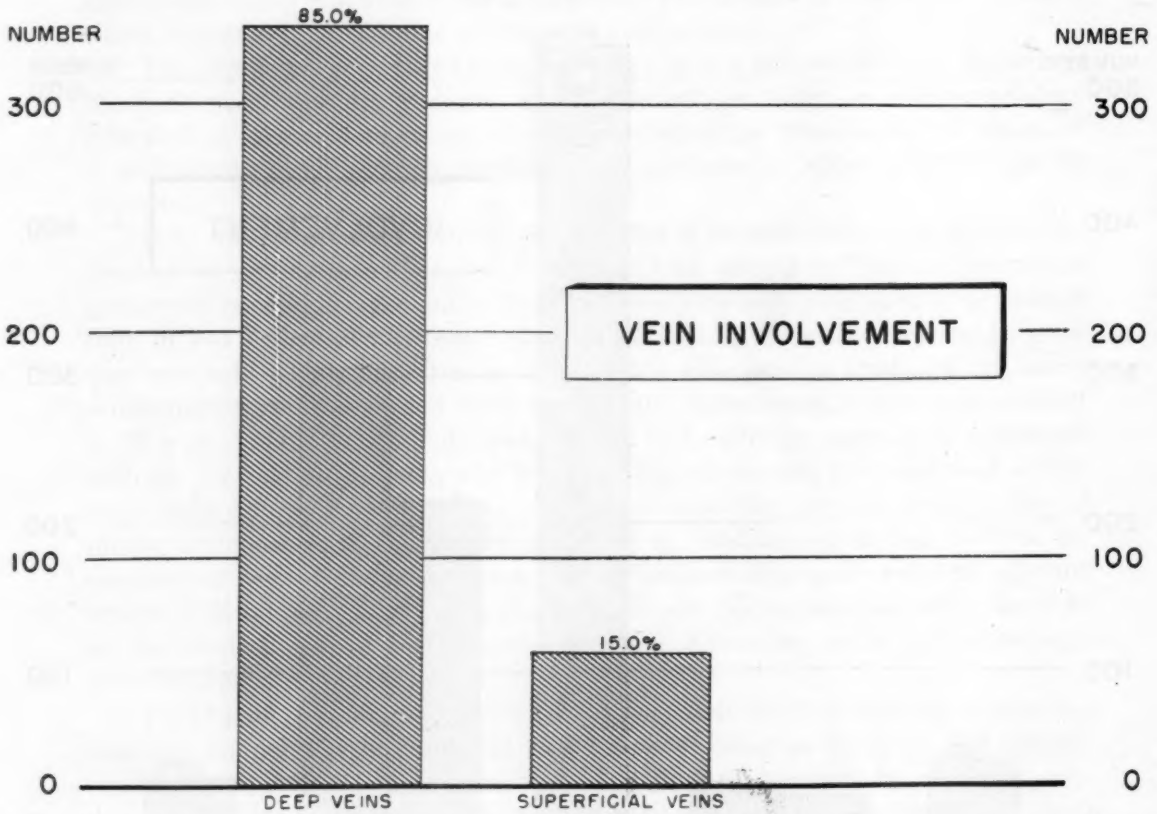

Fig. 6.

Site of Lesion.—The 502 patients with intravascular clotting in the Army series presented the lesion in 563 different sites. The lower extremity (Fig. 5). was involved more than thirteen times more often than the upper and the involvement in 29 instances was bilateral. The superior vena cava was the site of involvement in 3 instances.

In the 394 cases in the Army series in which this information was available (Fig. 6), the superficial veins were involved 59 times and the deep veins 335 times. In both the upper and the lower extremities the left side was more frequently involved than the right. The discrepancy may not be significant, but can be explained by the more marked circulatory retardation on this side, which is due to anatomic considerations: The right iliac artery crosses, and compresses

in the crossing, the left iliac vein, while the presence of the sigmoid and rectosigmoid on the left side may also play a part in the production of stasis in the common iliac vein.

There has been considerable discussion concerning the site of origin of thrombosis and embolism. Virchow,[196] who in 1846 published the first correctly interpreted instances of embolism, was of the opinion that the clot obstructing the pulmonary artery came from the pelvis or the lower extremities. Aschoff's[6] theory of thrombosis postulates the origin of fatal emboli in the femoral and iliac veins, but more recent observations are to the effect that many thromboses begin in the veins of the legs and feet.[13, 43, 70, 84, 85, 116, 138, 154, 166, 172] Neumann[138] described two clinical types of thrombosis, based on the site of origin, (1) a benign variety beginning in the veins of the legs and characterized by increased frequency with age, slow progression, and a tendency toward multiple but nonfatal emboli, and (2) a malignant variety, originating in the plantar veins and characterized by rapidly progressive thrombosis, occurrence in younger persons without increasing frequency with age, and a tendency toward the development of fulminating fatal pulmonary emboli.

SUPERIOR VENA CAVAL THROMBOSIS

The 3 instances of intravascular clotting in the superior vena cava observed in the vascular centers in the Zone of the Interior during World War II represent an unusual condition. Any variety of vena caval obstruction is rare; in 1933 Ehrlich, Ballon, and Graham[63] could find only 309 cases in the world literature. Obstruction due to thrombosis is even rarer; in 1936, Ochsner and Dixon[153] could find only 120 cases in the world literature, to which they added two personally observed cases. According to Zambellini[211] the first two reported cases of superior vena caval thrombosis were by Bartolino and Hunter.

In 95 of the cases collected by Ochsner and Dixon in which details of sex and race were given, there were 64 males and 92 white persons. The average age in 82 cases in which the age was stated was 43.6 years and the range was 9 to 74 years. In 13 cases the cause was either not stated or could not be determined. In 44 cases the condition followed phlebitis, in 35 external compression, and in 28 mediastinitis. All 3 of the Army cases were of spontaneous origin.

The clinical manifestations of thrombotic obstruction of the vena cava are the result of stasis in the tributaries draining into this vessel and are chiefly limited to the upper half of the body. Edema, the principal sign, is the result of stasis, deficient drainage, and transudation of fluid. The venous pressure is elevated, due to the obstruction and the necessity for spontaneous short-circuiting of the flow of blood. Edema of the eyelids is early and frequent, though often not conspicuous because collaterals develop early and because in the upright position drainage is good. It may extend to the face, particularly if the patient is recumbent for any length of time. Cyanosis of the face, especially of the lips and lobes of the ears, is a prominent feature in many cases and may be explained chiefly on the basis of anoxemia.[153] Other symptoms and signs include dyspnea,[203] cough, headache, vertigo, somnolence,[203] prominence of the eyes,[63] disturbances of vision, tinnitus, deafness, epistaxis,[63] hemoptysis, dysphagia, paresthesia, and

psychotic manifestations. Pleural effusions,[20] increased cerebrospinal fluid pressure, and varicosities are frequent. Venous hypertension in the upper extremities combined with normal venous pressure in the lower extremities is pathognomonic of the condition if it appears in association with edema and cyanosis of the face, neck, and upper extremities aggravated by recumbency.

The two principal types of vena caval obstruction, according to Carlson,[33] occur above and below the azygos vein. In the former type the azygos vein and its tributaries form the chief venous trunk for the return blood flow and the lower abdominal veins are relatively unimportant. In the latter type the superficial and deep abdominal plexuses are of greater importance and the return blood flow must be through the inferior vena cava. According to Wagner,[199] if dilated dorsothoracic superficial veins are present, the obstruction can be presumed to be below the azygos vein. Demonstrable collateral veins and other manifestations of superior vena caval obstruction are aggravated by exercise.

Clinical manifestations are dependent upon and directly proportionate to the rapidity with which thrombotic lesions form and collateral circulation develops. They are relatively few when the lesions develop slowly and an adequate collateral circulation has time to develop.

Treatment should, as far as possible, be based upon correction of the etiologic factor. Venesection[63, 153] may be helpful and mediastinotomy has been advocated[63, 153, 179] as a decompressive measure to permit recanalized vessels to function. The prognosis depends upon the rate at which the thrombosis forms and its extent, the rate at which the collateral circulation develops, and the adequacy of the collateral circulation. In the 120 cases collected by Ochsner and Dixon[153] from the world literature there were 85 deaths, or 75.9 per cent.

The 3 instances of vena caval thrombosis in the Army series illustrate most of the considerations described. The following history is typical.

CASE REPORT

A white man, 26 years of age, was first observed in the course of routine examination after induction for a minor illness. He had markedly dilated and tortuous superficial veins of both upper extremities and spider-web varicosities of the chest and axilla. In reply to specific questioning he stated that he suffered from fullness of the face and swelling beneath the eyes when he was straining and doing heavy work, as well as when he first awoke in the morning; at this time the lower eyelids felt full and puffy. He had himself noted the venous anomalies on the chest, axilla, and arms, and he thought that when the weather was warm there was possible swelling of the hands and fingers. He had completed basic training without difficulty, but for the past sixteen months had noted some shortness of breath when he was very active.

A phlebogram with diodrast disclosed marked dilatation of the veins in the chest, axilla, and upper arms. The spider-web varicosities observed clinically were found to extend bilaterally into the axillae and around the posterior shoulder regions, and dilated, tortuous veins extended downward toward the abdomen. In view of the moderate symptoms and signs no treatment was advised.

AXILLARY THROMBOSIS

Of 40 cases of thrombosis of the veins of the upper extremity (7.1 per cent), 28 (70 per cent) occurred in the axillary veins and the majority occurred on the

left side (58.6 per cent). Of the axillary thromboses, the right arm was affected in 71.4 per cent and the left in 28.6 per cent. In 7 cases of axillary thrombosis which I observed[90] at a single vascular center, the age range was from 20 to 37 years. The causes in these cases included climbing a rope, throwing rocks, twisting a propeller, carrying a bucket, and playing tennis. In one case there was no obvious cause. In other cases in the series and in cases reported in the literature the causes included grinding spark plugs, washing clothes, pulling up in bed, restraining a horse, swinging a golf club, pitching a baseball, lifting various heavy weights, and putting books on a shelf.[88] Evidently some sort of strain is necessary for its production.

The cases in this series followed the usual pattern. The onset varied from acute to gradual swelling. As a rule, pain was followed within several hours or several days by swelling and cyanosis. In the early stages arterial spasm was evident, and the hand was cold, blue, and edematous in many instances. In all cases the diagnosis was confirmed by phlebography, which showed the typical pattern of obstruction of the axillary vein.

Several theories have been advanced to explain axillary thrombosis. Von Schrotter,[198] who first described the condition in 1884, maintained that stretching of the vein caused a localized reaction which took the form of thrombosis. Cadenat[31] stated that the respiratory effort associated with strain distended the vein and produced a change in the intima which led to thrombosis. Lowenstein[109] contended that the position of abduction distended the vein and permitted pressure by the costocoracoid ligament and subclavian muscle. Gould and Patey[72] were of the same opinion and demonstrated, in addition, a valve at the level of the subclavius muscle which ruptures following pressure by the muscle on the axillary vein. Veal and McFetridge,[194] from studies on the cadaver, postulated compression of the vein below the head of the humerus against the subscapularis muscle. All of these theories are probably valid, but none explains the quiet type of thrombosis, which occurs without apparent cause. It may be that the thrombosis which develops during sleep is caused by prolonged compression of the vein induced by the position of the arm, particularly when it is elevated over the head or folded under the body. This position results in obstruction of the venous flow and reduction of the oxygen content of the blood, with changes in the intima which lead to thrombosis.[190]

The early arterial spasm present in axillary thrombosis is best treated by stellate ganglion block, repeated until pain and edema subside. In the 7 cases observed at the DeWitt General Hospital Vascular Center[90] this method was employed, in combination with extreme elevation of the extremity. The anterior approach for stellate ganglion block was used exclusively because of its ease of performance and the facility with which it can be taught.[151] If the method is employed early, it should prevent the lymphedema, which is the most disabling feature of this condition. As edema subsides, there is increased prominence of the superficial veins about the shoulder. The patients at DeWitt General Hospital, who were all seen late, showed no impressive change after repeated sympathetic blocks.

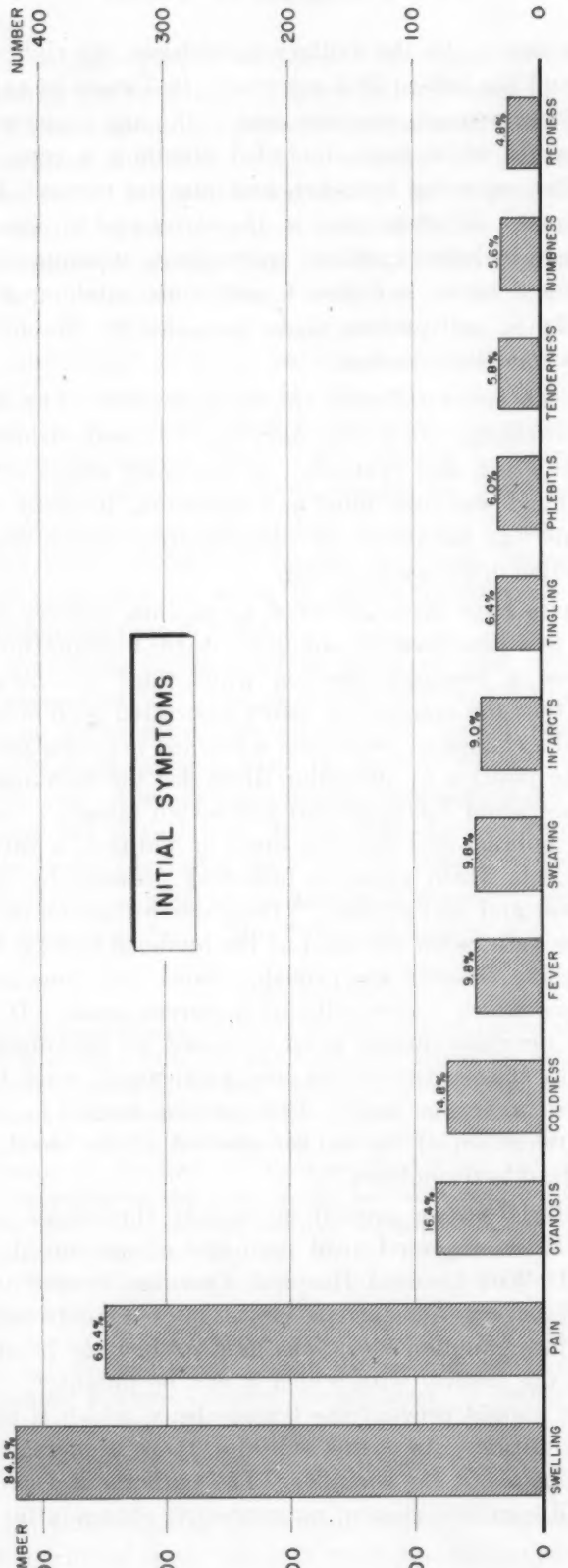
NUMBER
400
300
200
100
0
INITIAL SYMPTOMS
84.5%
69.4%
16.4%
14.8%
9.8%
9.8%
9.0%
6.4%
6.0%
5.8%
5.6%
4.8%
SWELLING
PAIN
CYANOSIS
COLDNESS
FEVER
SWEATING
INFARCTS
TINGLING
PHLEBITIS
TENDERNESS
NUMBNESS
REDNESS

Fig. 7.

CLINICAL PICTURE

The clinical picture is charted in Figs. 7 and 8. Swelling, which was present in 424 (84.5 per cent) of the 502 cases of intravascular clotting observed at the Army vascular centers, was the most prominent of the group of early symptoms, though it appeared first in only 140 cases (28 per cent). Pain, which was among the initial symptoms in 347 cases, was the first symptom in 174 (34.8 per cent). Cyanosis, which was among the initial symptoms in 82 cases, was the first symptom in only 5 cases. Coldness, which was among the initial symptoms in 74 cases, was not a first symptom in any case. Initial symptoms were always more marked in thrombophlebitis, because of its inflammatory character, and were slow and insidious in phlebothrombosis.

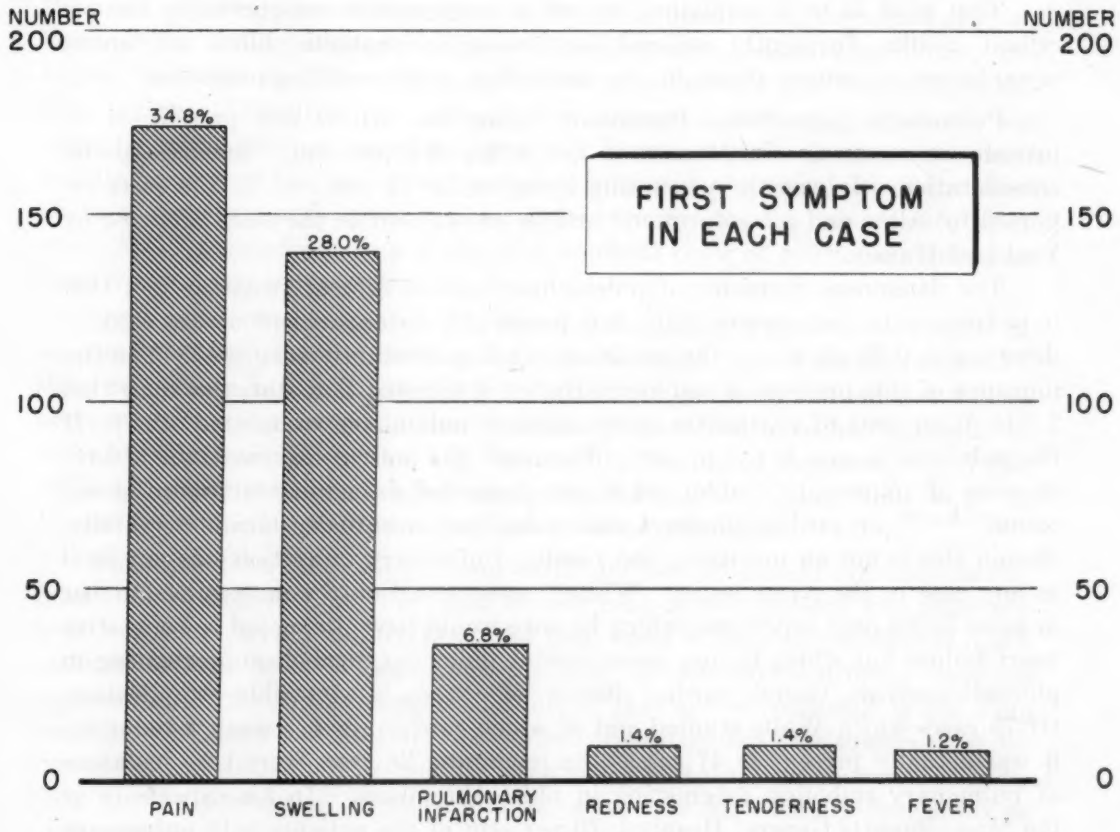

Fig. 8.

The origin of swelling, which is the most persistent and most disabling complication of intravenous clotting, is still a matter of considerable discussion. Originally the edema of thrombophlebitis was explained as due to increased venous pressure resulting from an obstructing thrombus. This factor probably does play a part in its production, but not as large a part in thrombophlebitis as in phlebothrombosis.

In thrombophlebitis not only the vein wall but also the perivenous tissues are involved in the inflammatory process. The surrounding reaction results in

lymphangitis,[83, 84, 89, 94] which results in turn in fibrinous exudation into the perivascular spaces. The clinical manifestation of accumulated exudation is edema. Recently it has been shown clinically[145, 147, 149] as well as experimentally[42] that edema in thrombophlebitis is secondary to severe arterial or peripheral reflex vasospasm originating in the affected segment. In severe cases vasospasm results in ischemia and explains the pallor of the skin which has long been recognized as a prominent feature in phlegmasia alba dolens. Loss of pulsation[156] in the affected blood supply also plays a part in the production of edema, which is increased because of stagnation, and the presence of which itself prevents absorption of the collected fluid. This hypothesis, as will be pointed out later, is supported by the excellent results obtained in many instances by lumbar sympathetic block.

That pain is to be explained by reflex vasospasm is supported by the excellent results frequently secured by lumbar sympathetic block. Cyanosis is explained by venous stasis due to obstruction, with resulting anoxemia.

Pulmonary Infarction.—Pulmonary infarction, which was present as an introductory symptom in 34 cases in this series (6.8 per cent), deserves special consideration. It was the presenting symptom in 41 per cent of the cases reported by Allen and his co-workers[2] and in 19 per cent of the cases reported by Veal and Hussey.[192]

The dangerous character of phlebothrombosis is evident from the fact that it is frequently unsuspected until this potentially fatal accident occurs. Early detection is difficult unless the condition is being constantly suspected. The significance of this problem is emphasized when it is noted that statistics show that 2.5 to 5 per cent of deaths are attributable to pulmonary embolism.[84, 85, 116] If the pulmonic process is not properly diagnosed, the patient may continue to have showers of pulmonary emboli, which are regarded as manifestations of pneumonia[80, 81, 206] or cardiac disease[14] and which may eventually terminate fatally, though this is not an inevitable end result. Pulmonary infarction was not fatal in any case in the Army series. White[206] commented on the increasing number of cases in his own experience which he once would have diagnosed as congestive heart failure but which he now recognizes as pulmonary embolism originating in phlebothrombosis, though cardiac disease, of course, is a possible complication. Of 75 cases which White studied and in which cardiac disease was a possibility, it was actually present in 47 cases; the remaining 28 cases were true instances of pulmonary embolism originating in phlebothrombosis. In his experience at the Massachusetts General Hospital, 70 per cent of the patients with pulmonary embolism of nonsurgical origin had symptomless clotting insidious in onset and situated in the deep veins.

Thrombosis begins in the deep veins of the leg and foot and may propagate and go on to embolism before it gives rise to marked clinical manifestations. It is necessary, if it is to be detected before complicating embolism occurs, that the possibility be borne constantly in mind. It should always be recollected as a possible development after operation, though the incidence is small, varying from 0.02 to approximately 1 per cent.[13, 75, 207] Detection is a matter of constant watchfulness. It involves repeated palpation of the extremities, the taking and

recording of serial comparative measurements, and repeated observations of the pulse rate, temperature, and respiration.[2, 48, 111, 142] Electrocardiography[8, 12, 39, 118, 126] may be very useful but opinions differ as to the value of phlebography.[2, 15, 56-58, 60, 66, 67, 90, 106, 112, 152, 174] I studied the serial phlebograms made in 110 cases of intravascular clotting at the DeWitt General Hospital Vascular Center[90] and concluded that they were of no value so far as early detection of phlebothrombosis was concerned and also of no value in identifying its location, even when the occurrence of pulmonary embolism had directed attention to its existence. My conclusion was that alert recollection of the possible occurrence of the condition is of far more value than any laboratory method.

The differential diagnosis of pulmonary embolism is frequently possible on the basis of periodic attacks of faintness, dyspnea, prostration, unexplained fever, leucocytosis, and sometimes jaundice. The diagnosis of massive pulmonary embolism, in which the patient goes into shock and dies within a few minutes, seldom presents difficulties. In patients who survive, atelectasis, pneumonia, and pleuritic effusions are secondary results. Roentgenologic diagnosis is disappointing except in the case of wedge-shaped infarctions.[74] Suspicion of the possibility of embolism and constant, close observation are the key to successful diagnosis, as I[90] pointed out in a study of 9 nonfatal cases of pulmonary embolism observed in Army personnel.

Once pulmonary infarction has directed attention to the existence of intravascular clotting, it is urgent that measures be taken to prevent its recurrence, since recurrence is a real possibility. Ziak,[213] for instance, pointed out that 70 per cent of patients who die from pulmonary embolism have had previous attacks of pulmonary infarction, and Graves,[73] in a study of 194 cases, found that while 140 patients had had only a single attack, some had had as many as 8. In 4 instances multiple emboli were not discovered until autopsy.

Not more than 20 to 25 per cent of all pulmonary emboli are immediately fatal. According to Ziak[213] at least 60 per cent of the patients live from one hour to several days. In only 45 of 154 fatal cases in Graves'[73] series did death occur within one hour or less. The remaining patients survived for at least one day, and some for longer periods of time, so that active treatment might have availed. DeTakats and Fowler[49] have also emphasized the fact that in most instances of embolism there is time for treatment, first during the actual episode, then for the prevention of other attacks, which are increasingly dangerous as their number increases. Approximately one-fifth to one-fourth of these emboli are fatal at the onset.

TREATMENT BEFORE ARRIVAL AT A VASCULAR CENTER

Treatment of the 502 patients in this series before their arrival at the vascular centers (Fig. 9) varied from bed rest in 228 cases, elevation in 141 (28.2 per cent), heat (28 per cent), sympathetic ganglion block (20 per cent), posterior tibial nerve block, typhoid, periarterial sympathectomy, and caudal anesthesia to sympathectomy in 10. The rationale of many of the methods utilized is obvious. Bed rest is employed because symptoms are increased with activity

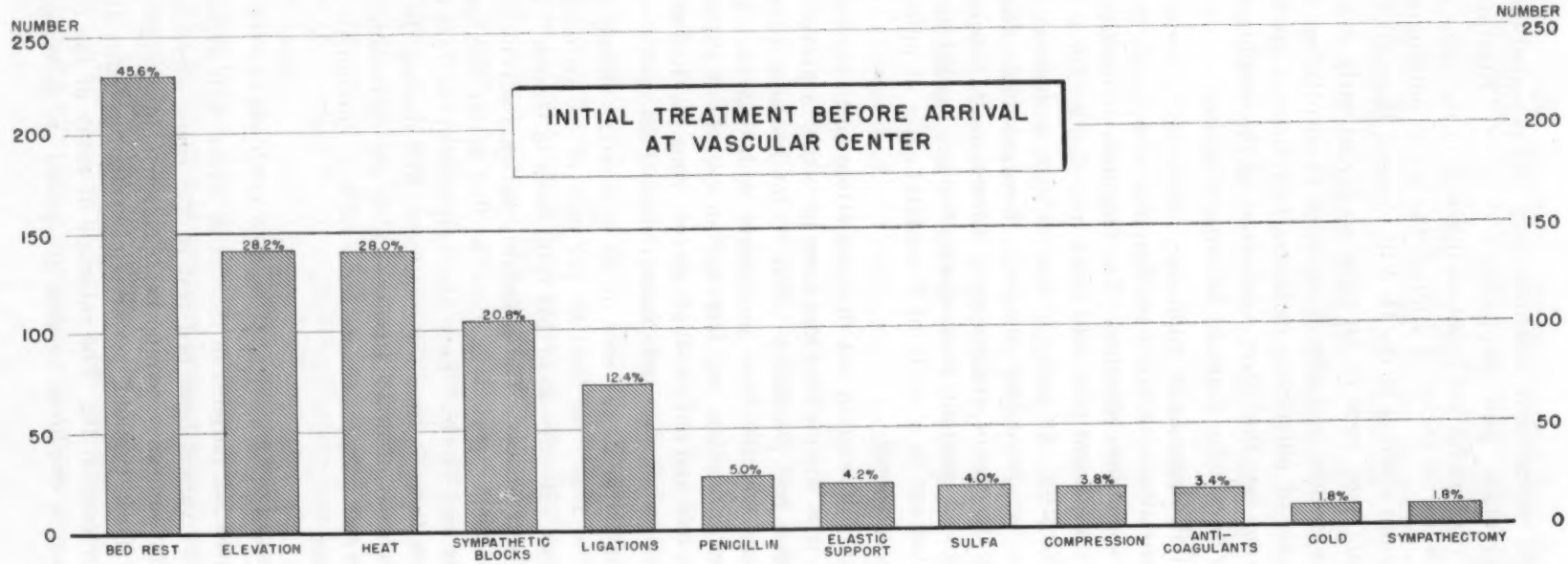
INITIAL TREATMENT BEFORE ARRIVAL AT VASCULAR CENTER
NUMBER
250
200
150
100
50
0
45.6%
28.2%
28.0%
20.8%
12.4%
5.0%
4.2%
4.0%
3.8%
3.4%
1.8%
1.8%
BED REST
ELEVATION
HEAT
SYMPATHETIC BLOCKS
LIGATIONS
PENICILLIN
ELASTIC SUPPORT
SULFA
COMPRESSION
ANTI-COAGULANTS
COLD
SYMPATHECTOMY

Fig. 9.

and the edema becomes more severe. Elevation of the limb enhances the return flow of blood and thus prevents edema. The rest are attempts to assure vasodilatation in some form and are most effective in acute thrombophlebitis because of the improvement produced in arteriolar pulsations and the resulting decrease in edema. The rationale of the objective has frequently been explained by Ochsner and DeBakey:[145, 147-149] The symptoms of thrombophlebitis are due to vasospasm, which affects venules as well as arterioles, and the methods to increase vasodilatation are therefore logical. Treatment is directed to the correction of the spasm which is not only arteriolar but also of the venule.[42] It has been shown[98, 103, 144] that postoperatively there is a peripheral vasoconstriction. In addition there is retardation of the circulation.[180] Once the thrombophlebitis has occurred treatment of vasospasm must be started.

SYMPATHECTOMY AND SYMPATHETIC BLOCK

In the Army series of 502 cases of intravenous clotting, sympathetic ganglion block had been done in 104 cases (20.8 per cent) before the patients arrived at vascular centers (Fig. 9), and it was done at the centers in 80 (16 per cent) additional cases (Fig. 12). The technique of stellate and of lumbar sympathetic block has been described elsewhere. I now prefer to use a single site for the injection, the second or third lumbar sympathetic ganglion. The results seem as good as when three sites are used, and the procedure is much less objectionable to the patient.

Results of sympathetic block vary. According to Ochsner and DeBakey,[144] who base their remarks on personal experience, complete relief can be expected within four days or less in 50 per cent of all cases and within five to eight days in another 30 per cent. Two-thirds of the patients can be discharged from the hospital within four to eight days after treatment is begun, and another 23 per cent within ten to twelve days. A follow-up study of their patients, covering six months to two years, revealed no recurrence of edema in any instance.

In 58 patients with deep femoral phlebitis treated by sympathetic block at Mayo General Hospital Vascular Center, relief of pain was accomplished in 21 cases and relief of pain and edema in 11. In 19 cases pain was not relieved. In 2 cases there was marked relief of vasospasm and in 2 cyanosis, sweating, pain, and edema were relieved. Permanent relief of edema was secured in 1 case. In 34 patients with deep thrombophlebitis observed at the DeWitt General Hospital Vascular Center,[90] all of whom were in the chronic stage, with durations varying from two months to twenty-four years, edema was an impressive and disabling sequel. Ten patients had been treated in the acute stage by lumbar sympathetic block, with dramatic relief from pain, but edema had not been effected, and it was greatly increased by dependency and activity. Generally speaking, sympathetic block is likely to be effective in the acute stage of intravascular clotting, when edema has not yet become fixed as a result of fibrosis and consequent lymphatic destruction, but is much less effective in the chronic stage, when these effects are evident. In 16 cases of chronic thrombophlebitis which I have studied,[90] improvement in the color of the affected extremity was observed after lumbar sympathetic block, but there was no change in the degree

of edema, and discomfort was also unaffected. The results in this small series seem to bear out the contention that while early treatment of vasospasm by sympathetic block frequently achieves brilliant results, edema will be permanently controlled only when the patient begins and continues to practice elevation of the part and to use an elastic support.

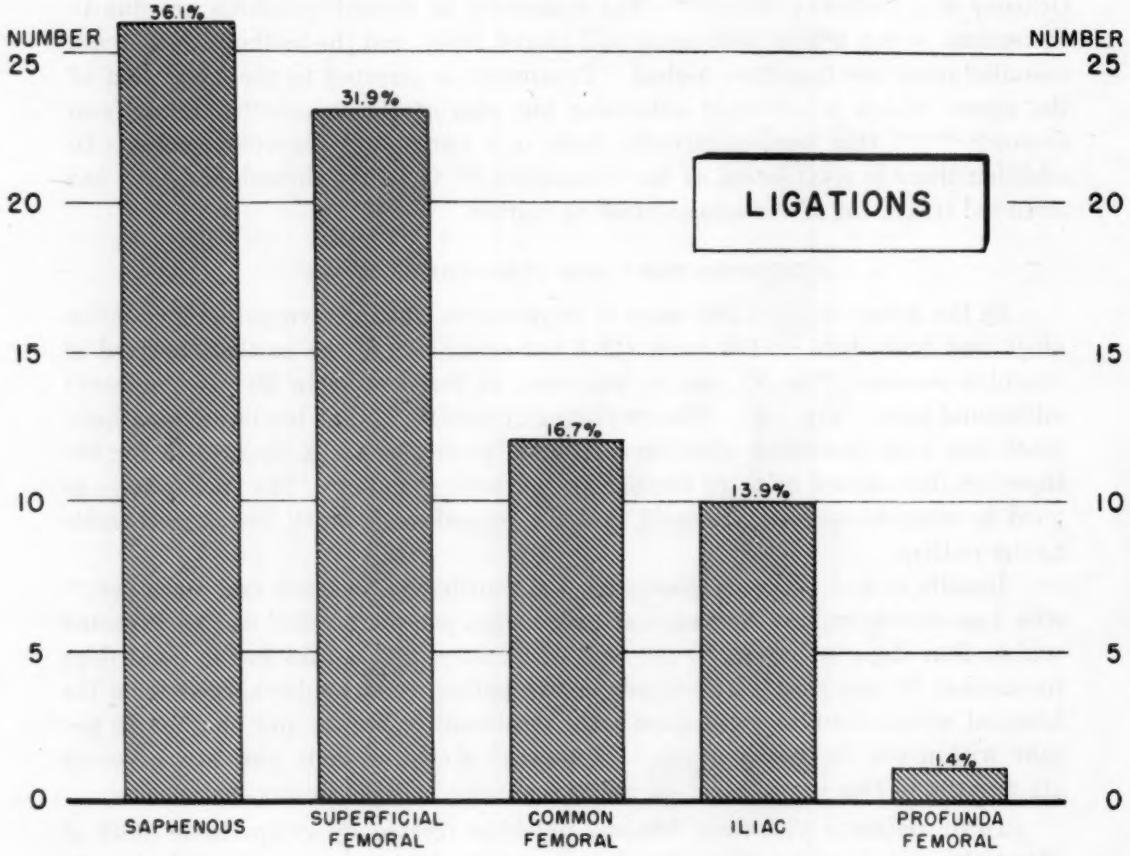

Fig. 10.

Lumbar sympathectomy was done in 15 cases of thrombosis of the deep veins on the indication of persistent pain, cold feet, sweating, and cyanosis. The effect on edema was not remarkable, though there was improvement in the patients' complaints of pain. In 1 instance of deep thrombophlebitis with edema which I observed, sympathectomy produced dramatic immediate relief from discomfort, but had no prolonged beneficial effect. The objective of sympathectomy is to achieve a permanent vasodilatation, but it is not indicated routinely and it should be done for the residuals of intravenous clotting only if a causalgic type of discomfort, excessive hyperhidrosis, and marked cyanosis are relieved by preliminary testing with lumbar sympathetic block.

VENOUS LIGATION

The venous ligations done in 72 cases (12.4 per cent) before the patients arrived at the vascular centers (Figs. 9 and 10), and done in one case at a cen-

ter, chiefly represent attempts to prevent propagation of quiet venous thromboses and the development of pulmonary emboli.[213]

Once the diagnosis of phlebothrombosis or thromboembolism is made, or even suspected, immediate measures to control it are essential, in the form of venous ligation proximal to the thrombosis, anticoagulant therapy, or both. It is essential that ligation be done above the site of the thrombosis. If the clot is definitely limited to the leg, it may be safe to ligate the superficial femoral vein distal to the profunda branch, but if there is any evidence of propagation, ligation must be done proximal to it. One is impressed by the frequent efforts reported to preserve the femoris profunda, but the attempt is not safe[67]; the site of the thrombosis may be in this very vein, and the patient may die of embolism if it is not tied off.[78] Frykholm[70] has shown that an independent thrombosis frequently originates in the veins of the deep muscles of the thigh and enters the common femoral vein by way of the profunda branches.

Homans[78] advocated ligation of the iliac vein because, for anatomic reasons, a better collateral circulation is available. If bilateral ligation of the femoral vein seems necessary, as many authorities believe when the site of the thrombosis cannot definitely be determined, he advocated ligation of the inferior vena cava. The first ligation of the inferior vena cava by Kocher[92] in 1883 and the second by Billroth[19] in 1885 were both done in error. The first successful deliberate ligation was reported by Bottini[24] in 1893. In 1937 Krotoski[96] was able to collect 48 cases from the literature, and Collins, Jones, and Nelson[36] have shown that the procedure is feasible and successful in a large proportion of cases. Since then many reports concerning the advisability of inferior vena caval ligation have been described in the literature.[124, 189, 193]

Fine and Sears[67] advised ligation of the common femoral vein because of the danger of embolism from the profunda vein when it was spared by ligation of the superficial femoral vein. In their opinion the iliac vein should be explored whenever there is clinical evidence of high thrombosis. If division of the femoral vein is done below the head of the thrombus, thrombectomy is necessary.[97, 101, 102, 146] In some clinics, since the site of the thrombosis in the lower extremity is difficult to determine, bilateral femoral vein ligation is being done.[1-3, 67, 79, 204]

Buxton and Coller[29] performed femoral vein ligation in 24 patients with deep phlebitis varying in duration from two months to thirty years. Most of the patients desired treatment because of chronic, recurrent ulceration about the ankle. A smaller number suffered from swelling, pain, and easy fatigue. Superficial varices were ligated before ligation of the femoral vein. These observers attempted to exclude patients with arteriosclerosis from femoral vein ligation, and did not perform the operation in patients more than 55 years of age. Results were disappointing when ligation was performed in the absence of stasis ulceration, but when ulcers were present there was a high incidence of healing, as well as marked relief of pain, although some lesions later recurred. One death followed complicating arterial disease and thrombosis. One patient required incision and drainage of a residual abdominal abscess four months after ligation of the femoral vein. Following the second operation, acute arterial embolism of

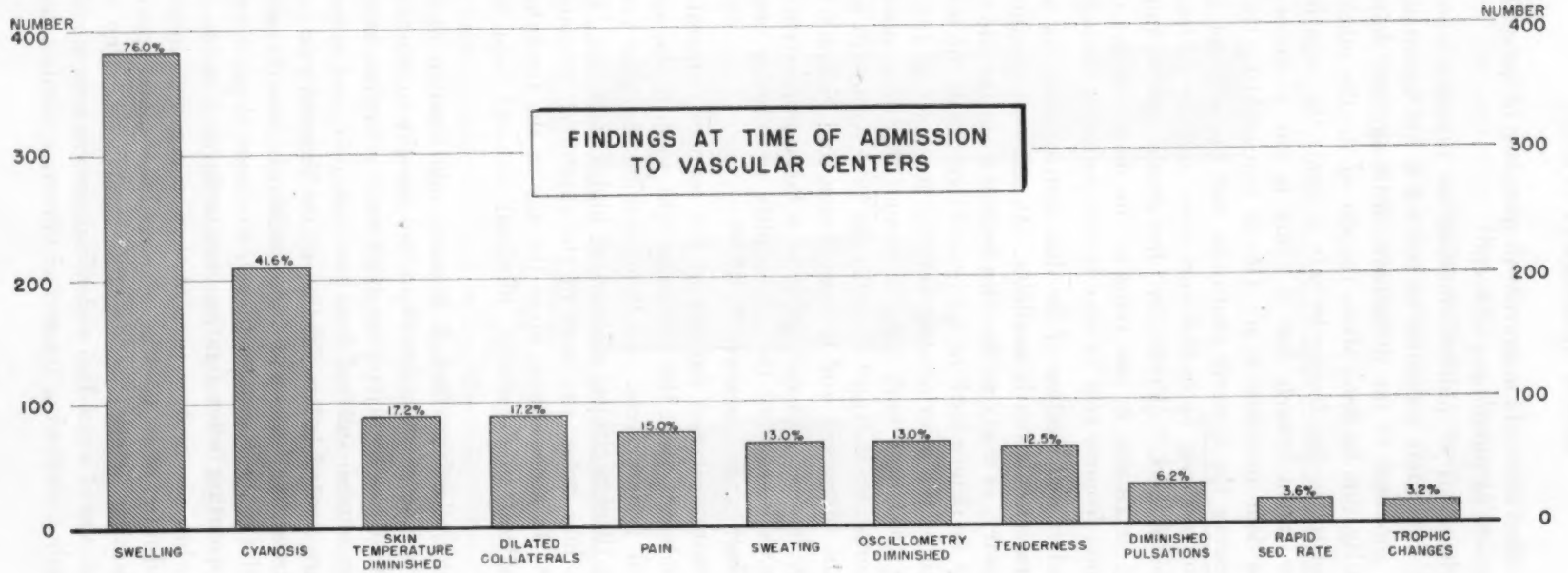
FINDINGS AT TIME OF ADMISSION TO VASCULAR CENTERS
NUMBER
400
300
200
100
0
76.0%
41.6%
17.2%
17.2%
15.0%
13.0%
13.0%
12.5%
6.2%
3.6%
3.2%
SWELLING
CYANOSIS
SKIN TEMPERATURE DIMINISHED
DILATED COLLATERALS
PAIN
SWEATING
OSCILLOMETRY DIMINISHED
TENDERNESS
DIMINISHED PULSATIONS
RAPID SED. RATE
TROPHIC CHANGES

Fig. 11.

the popliteal artery developed and amputation of the leg was necessary. One patient had more edema following femoral ligation than before. The collateral circulation became prominent and edema continued to increase until ligation of the vena cava was carried out, after which improvement was observed.

The details just presented suggest that treatment of deep phlebitis by ligation of the femoral vein is not entirely satisfactory. Certainly the method has not obtained general acceptance. The operation seems to have been performed first by Kraussold[95] for pyemia following infection of an amputation wound. In the majority of reported cases since that time the indications were acute processes such as suppurative thrombophlebitis, direct trauma to the vein, and phlebothrombosis. Homans felt it reasonable to assume that an old, sclerosed, canalized femoral or external iliac vein is better divided. Buxton and his co-workers[29, 30] explain the rationale on the basis that in thrombophlebitis there is destruction of the function of the valve. As a result, when the patient stands erect, blood pours down a valveless vein and returning blood must take, in part, collateral valved pathways which, when the phlebitic process is extensive, may themselves be in part incompetent. They endeavored to rectify the destroyed valvular system in the femoral vein by ligation of a portion of the femoroiliac system. The plan does not seem entirely rational, since division of the vein removes the remaining channel, while ligation and division of the varicose veins remove the only remaining pathways. The "persistent or increased swelling of the leg and thigh after operation," which the writers mention as a complication which has produced considerable concern, would seem almost inevitable under the circumstances. This point was also emphasized by Dennis,[44] who reported a case of femoral vein ligation for thrombophlebitis followed by pulmonary infarction and thrombosis in the opposite extremity. Dennis urged care in femoral vein ligation, in respect to destruction of the collateral veins left. I feel strongly that when femoral vein ligation is done, the collateral veins should be preserved, as they can be with the exercise of a little care.

Northway and Buxton[140] reported 10 instances of ligation of the inferior vena cava, 3 for multiple recent pulmonary emboli (in 1 instance associated with chronically recurrent edema and ulceration of the leg), 4 for chronic edema and ulceration, 2 for pain and edema, and 1 for epigastric pain associated with phlebothrombosis. Transection was done in 1 case. In the others the technique consisted of retroperitoneal exposure and ligation in continuity. Compression bandages were used after operation, and edema of the extremities was thus controlled after ambulation was begun. These writers were of the opinion that normal venous pressure cannot be expected in less than twelve months after operation.

Northway and Greenway[141] demonstrated on unembalmed cadavers the vascular alterations which follow this procedure. They ligated the superior vena cava at its entrance into the heart and removed the inferior vena cava from the region of the renal vein superiorly. The whole system was then irrigated by means of a cannula inserted into the femoral vein via the saphenous vein, in order to remove as much clotted blood as possible. The inferior vena cava was clamped just above the bifurcation and just below the renal veins; irrigation

was again carried out to cleanse the collateral system. Finally, a thin suspension of red lead was forced into the system under pressure for one minute, after which the cannula was removed and the saphenous vein was ligated. Roentgenologic studies and dissection of the injected venous channels showed that the collateral vessels were amply able to take over the functions of the ligated vena cava, which readily filled above the obstruction.

If the thrombosis is in the pelvic veins, Collins and his associates[36] were of the opinion that the uterine and ovarian veins should be ligated as well as the vena cava.

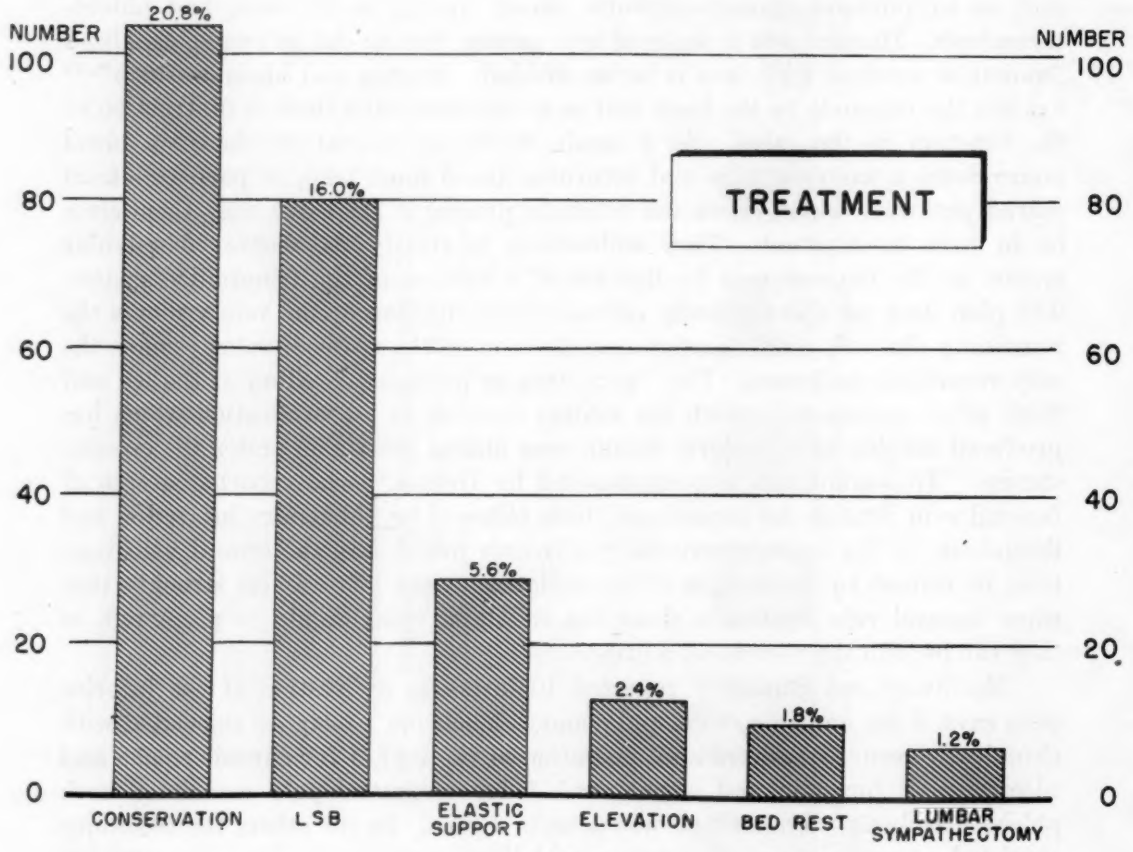

Fig. 12.

Veal and Hussey,[192] who observed 3 deaths from massive pulmonary embolism in cases of acute iliofemoral thrombophlebitis in which a new clot was engrafted on the old, expressed the opinion that there is danger of embolism in all cases of venous thrombosis for as long as four months afterward. Their preference is to perform venous ligation distal to the saphenous vein. In 45 cases they ligated one femoral vein, in 6 cases both, in 6 cases the external iliac, in 6 cases the inferior vena cava, and in 29 the common iliac. Despite their best efforts, there were 9 instances of embolism after ligation in the 45 cases in which ligation was performed before embolism was evident, but there was no further episode of pulmonary embolism in the 39 cases in which ligation was done after at least one episode of this kind.

Deep venous ligation was done in 72 (12.4 per cent) of the 502 cases of intravascular clotting which make up the Army series. It is noteworthy that in 21 instances of pulmonary embolism observed at the Mayo General Hospital, ligation had been done in only 5 cases; the remaining 16 patients recovered completely without specific therapy. Twelve patients of the 27 at the DeWitt General Hospital in whom venous ligation was done had pulmonary infarction prior to the operation but none developed it afterward, which suggests that adequate venous ligation is usually sufficient to prevent pulmonary infarction. Although many observers feel that ligation of the common femoral vein or ligation at a higher level is the method of choice in phlebothrombosis of the lower extremity, the majority of ligations in the Army series were done in the saphenous and the superficial femoral veins. No ligations of the vena cava were reported.

ANTICOAGULANT THERAPY

Anticoagulant therapy, in the form of dicoumarin, heparin, or both, was used in 17 cases in this series (3.4 per cent) with no untoward results. Theoretically, this prophylactic measure seems indicated in patients in whom there is a thrombosing tendency. Practically, the identification of such patients is difficult, though there has been renewed interest in the problem since the advent of anticoagulants.

When I[90] studied the bleeding and clotting times by the Lee and White method in 65 cases of intravascular clotting, I found no changes in the acute stage. Prothrombin time determinations also showed no variations from normal. Determinations on diluted plasma seem to detect a tendency toward increased clotting.[25] The latter method, however, requires a skilled laboratory technique. Estimation of the erythrocytic sedimentation rate has been used as an index of activity. DeTakats[46] found the response to heparin of patients with excessive coagulability of the blood to be strikingly diminished and recommended the use of the decreased heparin tolerance as a diagnostic test. However, in a study of 7 cases of intravenous clotting, I[90] was unable to confirm this and concluded that a better diagnostic aid was supplied by the erythrocytic sedimentation rate than by the heparin tolerance test.

DeTakats[46] stated that clotting factors have been known to exist in the postoperative state and in the presence of any kind of intravascular clotting. He supplied evidence that drugs like Prostigmine[47] or sulfur compounds[45] seemed to decrease the increased clotting factors. When there was an abnormal response,[45-47] it could be corrected by heparin, dicumarol, sulfur compounds, or prostigmine. In these cases, he uses anticoagulant therapy.

Although numerous observers have advised caution in the use of anticoagulants, there is considerable evidence of their value[4, 5, 22, 27, 40, 87, 99, 214] and, when they are properly used, of their safety. Dicumarol is favored, for it is less expensive than heparin. Reich and his associates[167] used it prophylactically in 102 surgical patients and Butsch and Stewart[27] used it in 23 male patients after hernioplasty. No patient developed either thrombosis or embolism, but 2 patients in the hernioplasty group developed hematomas in the wound.

Barker and his associates[12] gave dicumarol to 1,000 surgical patients in the immediate postoperative period. In patients with a history of thrombophlebitis or pulmonary embolism following previous surgery, and in cases in which abdominal hysterectomy or certain other operations were performed, the drug was begun approximately twenty-four hours after operation. They attempted to keep the prothrombin time between thirty-five and sixty seconds (against a normal of nineteen to twenty-two seconds) during the period in which intravascular thrombosis might develop. In the first 374 cases which these observers reported, pulmonary infarction developed in 1 case in which the prothrombin time was twenty-six seconds and thrombophlebitis in 1 case in which the prothrombin time was thirty-five seconds and in 1 in which it was forty-five seconds. Moderate or severe bleeding, with 2 exceptions, occurred only when the prothrombin time was above sixty seconds.

That anticoagulant therapy is not free from risk is evident in a number of reports in the literature. Evans,[64] who used dicumarol, heparin, or both in 56 cases of intravascular clotting, reported hemorrhagic phenomena in 8 cases and 2 deaths from bleeding, and Shlevin and Lederer[177] reported a death from uncontrollable hemorrhage after dicumarol therapy.

Yahr,[210] in an effort to evaluate dicumarol, treated 67 cases of thrombophlebitis by a uniform method. His series was divided as follows:

Eleven cases of superficial phlebitis: Wet boric acid dressings were applied locally. Pain was controlled by the administration of papaverine as necessary. The total average dose of dicumarol was 1,000 mg. During a follow-up period ranging from six to ten months there had been no recurrences.

Twenty-seven cases of deep phlebitis: The extremity was elevated and an icecap was applied at the point of maximum tenderness. When the patient was allowed out of bed, an elastic support was applied. Dicumarol was used in all cases. There were no instances of pulmonary embolism in the group.

Nine cases of superficial and deep thrombophlebitis: Treatment consisted of elevation of the extremity, wet dressings, papaverine, and dicumarol.

Ten cases of pulmonary embolism, in 8 of which the condition was postoperative: In 3 cases there were 2 episodes. Treatment consisted of sedation and dicumarol. No further episodes occurred.

In the whole group intravascular clotting developed after operation in 37 cases and either before or after delivery in 22. In the remaining cases the etiology was unknown. Yahr felt that in respect to length of treatment, lack of complications, absence of emboli, and wide margin of safety, dicumarol was a very satisfactory agent in the management of intravascular clotting.

Ochsner,[142] among others,[10, 41] has emphasized that the principal use of anticoagulants is prophylactic, and that when once thrombosis has occurred, this type of therapy has no effect on the lesion itself and merely serves to prevent propagation. Numerous successful cases have been reported. Reich and his associates[167] used dicumarol successfully in the treatment of 33 venous thromboses and 9 pulmonary embolisms which occurred in 2,591 surgical and obstetrical cases. Heparin was employed for the first twenty-four to forty-eight hours, since di-

cumarol does not become effective for this length of time. At the end of this period it was discontinued. Bauer[16, 17] used heparin in the treatment of thrombosis, and Priestly and Barker[164] used it in the treatment of 63 patients who developed thrombosis and embolism after operation and concluded that its proper use in patients in whom pulmonary embolism is not promptly fatal should prevent about one-third of the deaths which now occur from this condition. Other favorable reports were made by Wasserman and Stats[202] and by Pfeiffer and Sain.[158] Murray and his associates,[127-135] who have considerable clinical experience with heparin, reported a striking decrease in the incidence of postoperative embolism and in deaths from it following the use of this agent at the Toronto General Hospital, where originally over 10 per cent of all deaths were due to this complication, and where pulmonary emboli were found in 20 per cent of all post-mortem examinations.

Bancroft[9] expressed the opinion that the use of anticoagulants alone is not sufficient to protect patients against embolism. He reported 12 patients treated by heparin and thrombectomy, in 3 of whom simultaneous thrombectomies were performed on both iliac veins. There were 2 deaths in the series, 1 from thrombosis and 1 from postoperative renal insufficiency, and 1 patient later developed an embolism. It is well to emphasize that these drugs are more effective if used together.[168, 200]

EDEMA

The presence of edema in 380 of the 502 cases of intravascular clotting observed at the Army vascular centers is indicative of the importance of this complication. It is highly significant, furthermore, that it followed all types of initial therapy, including sympathetic block, sympathectomy, anticoagulant therapy, and venous ligation, and that it occurred regardless of whether the original condition was phlebothrombosis or thrombophlebitis.

It must be agreed, as already pointed out, that in acute thrombophlebitis, some measure to induce vasodilatation is necessary, and that if the pain is severe, a direct approach, such as is accomplished by regional sympathetic ganglion block, is effective. If phlebothrombosis is present, anticoagulant therapy or venous ligation, alone or in combination, should be employed, for the condition may give rise to an embolism which may be fatal. Anticoagulant therapy will preserve the collateral circulation, wholly or in part, and will prevent a marked degree of edema later, but the important consideration is the prevention of extension of the thrombus. Elevation of the extremity and the use of supporting bandages whenever the extremity is dependent will also have a favorable effect in the prevention of edema.

CONCLUSION

Intravenous clotting is far reaching in its complications and sequelae. It may result in persistent disabling edema or even death. A compiled series of 502 cases seen at the three vascular centers in the Army has been reviewed. Only 12 per cent presented no sequelae and 37.8 per cent were partially disabled (Fig. 13). The greatest offender was swelling. Chronic lymphedema is a

serious problem and is not to be regarded lightly. I believe that a proper evaluation of different types of treatment will relegate them to their proper spheres regardless of the enthusiasm of their proponents. It must be agreed that once acute thrombophlebitis ensues some form of vasodilatation is necessary. This will not always prevent the residuals of edema in a significant number of cases. If the condition is one of phlebothrombosis, adequate therapy to prevent embolism and propagation of the thrombosis are imperative. Even though the patient's life has been spared, the consequences of the venous obstruction are serious. I am firmly convinced that the major ingredient of any form of therapy

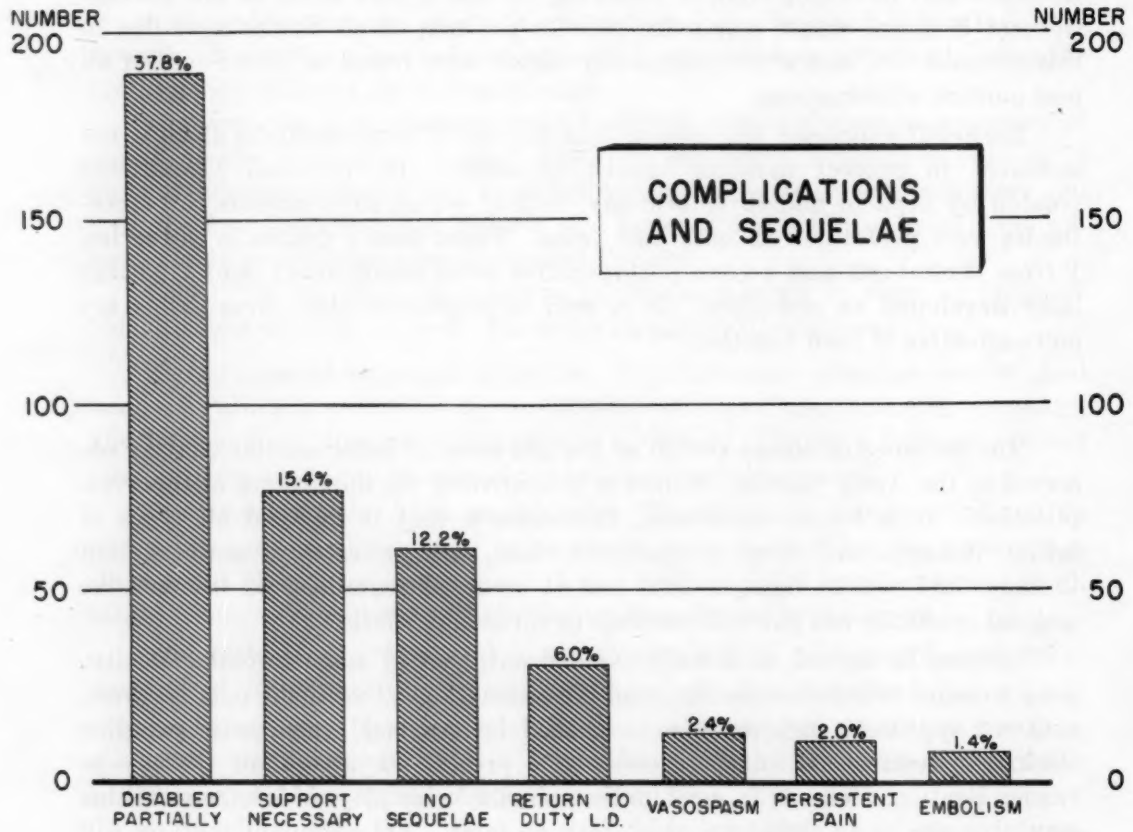

Fig. 13.

is the prevention of further thrombosis blocking an increasing number of collaterals. Obviously the end result regarding the edema will depend on the number of collaterals that are spared. The only means of prevention of propagation of the thrombus is by anticoagulant therapy and I am convinced that this should be started as soon as intravenous thrombus is evident regardless if other modes of therapy are chosen. This is not as applicable to acute thrombophlebitis as it is to phlebothrombosis. The golden period of treatment of lymphedema is immediate. This can be aided further by elevation at any time there is even the slightest suggestion of edema and the use of supportive bandages any time the extremity is dependent.

REFERENCES

1. Allen, A. W.: Interruption of the Deep Veins of the Lower Extremities in the Prevention and Treatment of Thrombosis and Embolism, Surg., Gynec. & Obst. **84**: 520-527, 1947.
2. Allen, A. W., Linton, R. R., and Donaldson, G. A.: Thrombosis and Embolism, Review of 202 Patients Treated by Femoral Vein Interruption, Ann. Surg. **118**: 728-740, 1943.
3. Allen, A. W., Linton, R. R., and Donaldson, G. A.: Venous Thrombosis and Pulmonary Embolism, J. A. M. A. **133**: 1268-1274, 1947.
4. Allen, E. V., Barker, N. W., and Waugh, J. M.: A Preparation From Spoiled Sweet Clover (3,3′-Methylene-Bis (4-Hydroxycoumarin)) Which Prolongs Coagulation and Prothrombin Time of the Blood: A Clinical Study, J. A. M. A. **120**: 1009-1015, 1942.
5. Allen, E. V.: The Clinical Use of Anticoagulants, Report of Treatment With Dicoumarol in 1686 Postoperative Cases, J. A. M. A. **134**: 323-329, 1947.
6. Aschoff, L.: Ueber Thrombose und Embolie, Wien. klin. Wchnschr. **51**: 1277-1282, 1938. Aschoff, L.: Thrombosis: Lectures on Pathology, New York, 1924, Paul B. Hoeber, Inc.
7. Aycock, T. B., and Hendrick, J. W.: The Problem of Venous Thrombosis, J. A. M. A. **133**: 1259-1263, 1947.
8. Baker, E. C., and Miller, F. A.: Further Experiences With Venography, Radiology **43**: 129-134, 1944.
9. Bancroft, F. W.: Proximal Ligation and Thromboectomy for Phlebothrombosis of the Femoral and Iliac Veins, Ann. Surg. **121**: 175-184, 1945.
10. Barker, N. W., Allen, E. V., and Waugh, J. M.: Use of Dicoumarol in the Prevention of Postoperative Thrombophlebitis and Pulmonary Embolism, Proc. Staff Meet., Mayo Clin. **18**: 102-107, 1943.
11. Barker, N. W., and Counseller, V. S.: Prevention and Treatment of Postoperative Thrombophlebitis, Am. J. Obst. & Gynec. **37**: 644-653, 1939.
12. Barker, N. W., Cromer, H. E., Hurn, M., and Waugh, J. M.: The Use of Dicoumarol in the Prevention of Postoperative Thrombosis and Embolisms With Special Reference to the Dosage and Safe Administration, SURGERY **17**: 207-218, 1945.
13. Barker, N. W., Nygaard, K. K., Walters, W., and Priestly, J. T.: A Statistical Study of Postoperative Venous Thrombosis and Pulmonary Embolism, Proc. Staff Meet., Mayo Clin. **15**: 769-773, 1940; **16**: 17-21, 33-37, 1941.
14. Barnes, A. R.: Pulmonary Embolism, J. A. M. A. **109**: 1347-1353, 1937.
15. Bauer, G.: A Venographic Study of Thromboembolic Problems, Acta chir. Scandinav. (Supp.) **84**: 1, 1940.
16. Bauer, G.: Heparin as a Therapeutic Against Thrombosis; Results of One Year's Treatment at Mariestad Hospital, Acta chir. Scandinav. **86**: 267-286, 1942; J. A. M. A. **120**: 1166, 1942.
17. Bauer, G.: Heparin Therapy in Acute Deep Venous Thrombosis, J. A. M. A. **131**: 196-203, 1946.
18. Belt, T. H.: Thrombosis and Pulmonary Embolism, Am. J. Path. **10**: 129-144, 1934.
19. Billroth, cited by Pfaff, O. G.: Ligation of Inferior Vena Cava, Am. J. Obst. & Gynec. **11**: 660-663, 1926.
20. Bittman, R. B.: Thymoma and Exploratory Thoracotomy, S. Clin. North America **112**: 1265, 1932.
21. Blair, B., in discussion of Glynn, E. E.: Pulmonary Embolism and Primary Pulmonary Thrombosis, J. Obst. & Gynaec., Brit. Emp. **31**: 521, 1924.
22. Bollman, J. L., and Preston, F. W.: Effects of Experimental Administration of Dicoumarin, J. A. M. A. **120**: 1021, 1942.
23. Boldt, H. J.: The Management of Laparotomy Patients and Their Modified Treatment, N. York M. J. **85**: 145-153, 1907.
24. Bottini, cited by Costa, G.: Arch. ital. di chir. **4**: 339-388, 1921.[140]
25. Brambel, C. E., and Loher, F. F.: Significance of Variations of Prothrombin Activity of Diluted Plasma, Proc. Soc. Exper. Biol. & Med. **53**: 218, 1943.
26. Burke, M.: Thrombosis: A Medical Problem, Am. J. M. Sc. **196**: 796-814, 1938.
27. Butsch, W. L., and Stewart, J. D.: Administration of Discoumarin Compound for Prophylaxis of Postoperative Thrombosis and Embolism, Arch. Surg. **45**: 551, 1942.
28. Butt, H. R., Allen, E. V., and Bollman, J. L.: A Preparation From Spoiled Sweet Clover Which Prolongs Coagulation and Prothrombin Time of the Blood; Preliminary Reports of Experimental and Clinical Studies, Proc. Staff Meet., Mayo Clin. **16**: 388-395, 1941.
29. Buxton, R. W., and Coller, F. A.: Surgical Treatment of Long-Standing Deep Phlebitis of the Leg—A Supplementary Report, SURGERY **18**: 663-669, 1945.
30. Buxton, R. W., Farris, J. J., Moyer, C. A., and Coller, F. A.: Surgical Treatment of Long-Standing Deep Phlebitis of Leg, A Preliminary Report, SURGERY **15**: 749-756, 1944.

31. Cadenat, F. M.: Les thrombophlebitis des membre supérieûre, Paris méd. **35**: 253-259, 1920.
32. Campeanu: Cited by Zava.[212]
33. Carlson, H. A.: Superior Vena Cava Obstruction, Proc. Soc. Exper. Biol. & Med. **30**: 293, 1932-3.
Idem: Obstruction of the Superior Vena Cava: An Experimental Study, Arch. Surg. **29**: 669, 1934.
34. Chiasserini, A.: Cause e meccanismi delle postoperatorie, Cong. Soc. internat. de chir., Rap. **1**: 3, 377, 1929-1930.
35. Coley, B. L.: Incidence of Phlebothrombosis and Embolism in Thirty Hospitals in the Eighth Service Command. Meeting of the Surgical and Orthopedic Consultants of the Service Commands, Surg., Gynec. & Obst., 10-11, 1944.
36. Collins, C. G., Jones, J. R., and Nelson, E. W.: Surgical Treatment of Pelvic Thrombophlebitis: Ligation of Inferior Vena Cava and Ovarian Veins: Preliminary Report, New Orleans M. & S. J. **95**: 324-329, 1943.
37. Copley, A. L., and Stefko, P. L.: Coagulation Thrombi in Segments of Artery and Vein in Dogs and the Genesis of Thromboembolism, Surg., Gynec. & Obst. **84**: 451-459, 1947.
38. Culp, O. S.: Postoperative Venous Thrombosis and Pulmonary Embolism: Analysis of Thirty-eight Cases, Bull. Johns Hopkins Hosp. **67**: 1-24, 1940.
39. Currens, J.: Electrocardiogram in Pulmonary Embolism, Proc. Staff Meet., Mayo Clin. **17**: 502-509, 1942.
40. D'Alessandro, A. J.: Heparin: Its Properties and Clinical Use, Collective Review, Internat. Abstr. Surg. **74**: 62-69, 1942.
41. DeBakey, M.: Dicoumarin and Prophylactic Anticoagulants in Intravascular Thrombosis, SURGERY **13**: 456-459, 1943.
42. DeBakey, M., Burch, G. E., and Ochsner, A.: Effect of Chemical Irritation of Venous Segment on Peripheral Pulse Volume, Proc. Soc. Exper. Biol. & Med. **41**: 585-590, 1939.
43. Deneche, K.: München. med. Wchnschr. **76**: 1912, 1929, cited by McCartney.[116]
44. Dennis, C.: Disaster Following Femoral Vein Ligation for Thrombophlebitis; Relief by Fasciotomy; Clinical Case of Renal Impairment Following Crush Injury, SURGERY **17**: 264-269, 1945.
45. DeTakats, G.: The Effect of Sulfur Compounds on Blood Clotting, SURGERY **14**: 661, 1943.
46. DeTakats, G.: Heparin Tolerance. A Test of the Clotting Mechanism, Surg., Gynec. & Obst. **77**: 31, 1943.
47. DeTakats, G.: The Nervous Regulation of the Clotting Mechanism, Arch. Surg. **48**: 105, 1944.
48. DeTakats, G.: Postoperative Thrombosis and Embolism, Illinois M. J. **79**: 25-32, 1941.
49. DeTakats, G., and Fowler, E. F.: The Problem of Thrombo-Embolism, SURGERY **17**: 153-177, 1945.
50. DeTakats, G., and Jeser, J. H.: Pulmonary Embolism; Suggestions for Its Diagnosis, Prevention, and Management, J. A. M. A. **114**: 1415, 1940.
51. DeTakats, G., Mayne, A., and Peterson, W. F.: The Meterologic Factor in Pulmonary Embolism, SURGERY **7**: 819-827, 1940.
52. DeTakats, G., Trump, R. A., and Silbert, N. C.: The Effect of Digitalis on Blood Clotting, J. A. M. A. **125**: 840, 1944.
53. deTorres, M.: Phlébites et embolies consécutives aux opérations gynécologiques, Progrès méd., 1609, 1934; Phlebitis and Embolism Following Gynecologic Operations, J. A. M. A. **103**: 1865, 1934.
54. Dock, W.: The Use and Abuse of Bedrest: Conferences of Therapy New York Hospital, New York State J. Med. **44**: 724-730, 1940.
55. Domrich, H.: Deutsche Ztschr. f. Chir. **222**: 20, 1930, cited by McCartney.[116]
56. Domrich, H.: Phlebegraphic directe: conception, technique, premiers resultants, J. Int. de chir. **6**: 625, 1938.
57. dos Santos, J. C.: Phlebographie d'uns veins cave inferieuse suturee, J. d'urol **39**: 588, 1933.
58. dos Santos, J. C.: Spasme vieneux du bras après injection intraartérielle: action de l'infiltration du ganglion étoilé: contrôle phlébographique avant et après l'infiltration, Rev. de chir., Paris **76**: 308-314, 1938.
59. Dougal, D.: The Etiology of Thrombosis and Embolism, J. Obst. & Gynaec. Brit. Emp. **45**: 425-450, 1938.
60. Dougherty, J., and Homans, J.: Venography, A Clinical Study, Surg., Gynec. & Obst. **71**: 697-702, 1940.
61. Duval, P., and Binet, L.: Essai Expérimental sur la pathogénie de certaines complications post-opératoires, Mem. Acad. de chir. **62**: 181-192, 1936.[146]

62. Duval, P., Roux, J. C., and Goiffon, R.: Essai sur l'intoxication par les polypeptides, Presse méd. **42**: 1785-1787, 1934.[146]
63. Ehrlich, W., Ballon, H. C., and Graham, E. A.: Superior Vena Caval Obstruction With a Consideration of the Possible Relief of Symptoms by Mediastinal Decompression, J. Thoracic Surg. **3**: 352, 1933.
64. Evans, J. A.: Dicoumarol Therapy in Thrombotic Emergencies, New England J. Med. **230**: 131-135, 1944.
65. Ewald, C.: Therapie der Thrombophlebitis und der Thromboembolie, Wien. klin. Wchnschr. **50**: 377, 1937.
66. Fine, J., Frank, H. A., and Starr, A.: Recent Experiences With Thrombophlebitis of the Lower Extremity and Pulmonary Embolism, Ann. Surg. **116**: 574-595, 1942.
67. Fine, J., and Sears, J. B.: The Prophylaxis of Pulmonary Embolism by Division of the Femoral Vein, Ann. Surg. **114**: 801-812, 1941.
68. Flörcken, H.: Aussprache über die Behandlung der Venenthrombose bei drohender oder bestehender Embolie, Med. Klin. **36**: 244, 1940.[146]
69. Frauendorfer: Cited by Müller-Meernach.[125]
70. Frykholm, R.: Pathogenesis and Mechanical Prophylaxis of Venous Thrombosis, Surg., Gynec. & Obst. **71**: 307-312, 1940.
71. Gordon-Watson, C.: In discussion of Lockhart-Mummery.[107]
72. Gould, E. P., and Patey, D. H.: Primary Thrombosis of the Axillary Vein, Brit. J. Surg. **16**: 208-213, 1928.
73. Graves, W. N.: Pulmonary Embolism. A Statistical Review of Cases From 1929 Through 1938, Surg., Gynec. & Obst. **70**: 958-963, 1940.
74. Hampton, A. O., and Castleman, B.: Correlation of Postmortem Chest Teleroentgenograms With Autopsy Findings, Am. J. Roentgenol. **43**: 305, 1940.
75. Heard, J. E.: Papers Mayo Clinic and Mayo Staff **2**: 419, 1923.
76. Henderson, E. F.: Fatal Pulmonary Embolism: A Statistical Review, Arch. Surg. **15**: 231, 1927.
77. Homans, J.: Circulatory Diseases of the Extremity, New York, 1939, The Macmillan Company.
78. Homans, J.: Exploration and Division of the Femoral and Iliac Veins in the Treatment of Thrombophlebitis of the Legs, New England J. Med. **224**: 179-186, 1941.
79. Homans, J.: Deep Quiet Venous Thrombosis in the Lower Limb, Preferred Levels for Interruption of Veins: Iliac Section or Ligation, Surg., Gynec. & Obst. **79**: 70-82, 1944.
80. Homans, J.: Diseases of the Veins, Venous Thrombosis and Pulmonary Embolism, New England J. Med. **231**: 51-60, 1944.
81. Homans, J.: Pulmonary Embolism Due to Quiet Venous Thrombosis and Simulating Cardiac and Pulmonary Disease, New England J. Med. **229**: 309, 1943.
82. Homans, J.: Venous Thrombosis and Pulmonary Embolism, New England J. Med. **236**: 196, 1947.
83. Homans, J., and Zollinger, R.: Experimental Thrombophlebitis, Arch. Surg. **18**: 992, 1929.
84. Hunter, W. C., Krygier, J. J., Kennedy, J. C., and Sneeden, V. D.: Etiology and Prevention of Thrombosis of the Deep Leg Veins: Study of Four Hundred Cases, SURGERY **17**: 178-190, 1945.
85. Hunter, W. C., Sneeden, V. D., Robertson, T. D., and Snyder, G. A. C.: Thrombosis of the Deep Veins of the Legs; Its Clinical Significance as Exemplified in Three Hundred and Fifty-one Autopsies, Arch. Int. Med. **68**: 1-17, 1941.
86. Jensen, D. R.: The Problem of Thrombophlebitis, Ann. Surg. **121**: 314-327, 1945.
87. Jorpes, J. E.: Anticoagulant Therapy in Thrombosis, Surg., Gynec. & Obst. **84**: 677-681, 1947.
88. Kaplan, T.: Thrombosis of the Axillary Vein, SURGERY **12**: 184-191, 1942.
89. Karsner, H. T.: Human Pathology, Philadelphia, 1926, J. B. Lippincott Company.
90. Kleinsasser, L. R. J.: The Present Concept of Phlebothrombosis, Thrombophlebitis, and Pulmonary Embolism, California & West. Med. **64**: 18-29, 1946.
91. Koch, Cited by Müller, A.: Die Thrombophlebitis und ihre Behandlung mit Komprimierendem Gehverband, Med. Klin. **33**: 793-797, 1937.[146]
92. Kocher, cited by Pfaff, O. G.: Am. J. Obst. & Gynec. **11**: 660-663, 1926.
93. Koenig: Cited by Müller-Meernach.[125]
94. Koester: Inaugural Dissertations, Bonn, 1870, cited by Ochsner.[142]
95. Kraussold, H.: Ueber eine operative Methode zur Bekämpfung beginnender Pyaemie, Arch. f. klin. Chir. **22**: 965-973, 1878.[146]
96. Krotoski, J.: Zur Venenunterbindung bzw.-exstirpation bei der puerperalen Allgemeininfektion von chirurgischen Standpunkt, Chirurg **9**: 425-439, 1937.[146]
97. Kulenkampff, D.: Die Verhütung schwerer oder tödlicher Embolien durch Ausräumung der V. iliaca, Zentralbl. f. Chir. **62**: 1258, 1938.

98. Kvale, cited by Ward, C. E., and Horton, B. T.: Postoperative Thrombophlebitis of Inferior Vena Cava in Child, Proc. Staff Meet., Mayo Clin. **12**: 811-814, 1937.
99. Lam, C.: Heparin Administration, Methods and Results in Thirty Cases, Ann. Surg. **114**: 205-211, 1941.
100. Lambret, O., and Driessens, J.: L'hyperpolypeptidémie secondaire aux opérations chirurgicales, Compt. rend. Soc. de biol. **104**: 567-568, 1930.[146]
101. Lange, K.: Beitrag zur operativen Behandlung der blanden Venenthrombose, Zentralbl. f. Chir. **65**: 2422-2425, 1938.
102. Läwen, A.: Arteriospasmus bei akuter massiver Thrombose der V. femoralis, Zentralbl. f. Chir. **61**: 1681-1685, 1934.
103. Leriche, R.: Des moyens de rédiure au minimum la maladie postopératoire; de l'operation sous rayons infra rougees, Rev. de Chir. Paris **74**: 99-108, 1936.[142]
104. Leriche, R.: The Prognosis and Treatment of Large Emboli of the Pulmonary Artery, Lyon chir. **41**: 257, 1946. Internat. Abstract Surg. (Surg., Gynec. & Obst. **84**: 382, 1947.
105. Leriche, R., and Kunlin, J.: Traitement immédiat des phlébites post-opératoires par l'infiltration novocaïnique du sympathique lombaire, Presse méd. **42**: 1481, 1934.
106. Lesser, A., and Danelius, G.: Venography: Its Value in the Diagnosis and Management of Venous Disturbances of the Lower Extremities, Ann. Surg. **119**: 903, 1944.
107. Lockhart-Mummery, P.: Discussion on Postoperative Pulmonary Embolism, Brit. M. J. **2**: 850-857, 1924.
108. Loewe, L., and Hirsch, E.: Heparin in the Treatment of Thromboembolic Disease, J. A. M. A. **133**: 1263-1268, 1947.
109. Lowenstein, P. S.: Thrombosis of the Axillary Vein: An Anatomic Study, J. A. M. A. **82**: 854-857, 1924.
110. Luckhardt, A. B., Alpert, R., and Smith, S.: Hemodynamic and Respiratory Changes Following Manipulation and Traction of the Gastrohepatic Ligament, Science **76**: 545, 1932.
111. Mahler, cited by Kulenkampff, D.: Die Verhütung schwerer oder todlicher Embolien durch Ausräumung der V. iliaca, Zentralbl. f. Chir. **62**: 1258, 1938.
112. Mahorner, H.: Method for Obtaining Venograms of the Veins of the Extremities, Surg., Gynec. & Obst. **76**: 41-42, 1943.
113. Martland, H. S.: Static or Spontaneous Thrombosis of Veins of Lower Extremity and Pelvis, and Fatal Pulmonary Embolism Following Trauma and Surgical Operations, S. Clin. North America **21**: 383-407, 1941.
114. Mason, E. C.: Blood Coagulation: The Production and Prevention of Experimental Thrombosis and Pulmonary Embolism, Surg., Gynec. & Obst. **39**: 421-428, 1924.
115. Matas, R.: Postoperative Thromboses and Pulmonary Embolism Before and After Lister, Donald C. Balfour Lecture in Surgery, Univ. Toronto M. Bull. **10**: 1, 1932.
116. McCartney, J. S.: Postoperative Pulmonary Embolism, SURGERY **17**: 191-206, 1945.
117. McCartney, J. S.: Pulmonary Embolism: A Report of Seventy-three Cases, Arch. Path. **3**: 921-927, 1927.
118. McGinn, S., and White, P. D.: Acute Cor Pulmonale Resulting From Pulmonary Embolism, J. A. M. A. **104**: 1473-1480, 1935.
119. McPheeters, H. O.: Femoro-iliac Thrombosis and Thrombophlebitis, Minnesota Med. **21**: 200-223, 1938.
120. Meade, W. H., and Ochsner, A.: Spool Cotton as Suture Material, J. A. M. A. **113**: 2230, 1939.
121. Miller, R. H., and Rogers, H.: Embolism and Phlebitis, J. A. M. A. **93**: 1452, 1929.
122. Moran, T. J.: Pulmonary Embolism in Nonsurgical Patients With Prostatic Thrombosis, Am. J. Clin. Path. **17**: 205-208, 1947.
123. Morton, J. J., Mahoney, E. B., and Mider, G. B.: An Evaluation of Pulmonary Embolism Following Intravascular Venous Thrombosis, Ann. Surg. **125**: 590-600, 1947.
124. Moses, W. R.: Ligation of the Inferior Vena Cava or Iliac Veins, New England J. Med. **235**: 2, 1946.
125. Müller-Meernach, O.: Zur Frage der Prophylaxe der postoperativen Thrombose und Embolie, München. med. Wchnschr. **83**: 1880, 1936; **84**: 1169, 1937.
126. Murnaghan, D., McGinn, S., and White, P. D.: Pulmonary Embolism With and Without Acute Cor Pulmonale, With Especial Reference to Electrocardiogram, Am. Heart J. **25**: 573-597, 1943.
127. Murray, G.: Heparin in Thrombosis and Blood Vessel Surgery, Surg., Gynec. & Obst. **72**: 340-344, 1941.
128. Murray, G.: Heparin in Surgical Treatment of Blood Vessels, Arch. Surg. **40**: 307-325, 1940.
129. Murray, G.: Aortic Embolectomy, Surg., Gynec. & Obst. **77**: 157-162, 1943.
130. Murray, G.: Anticoagulants in Venous Thrombosis and the Prevention of Pulmonary Embolism, Surg., Gynec. & Obst. **84**: 665-669, 1947.

131. Murray, G., and Best, C. H.: The Use of Heparin in Thrombosis, Ann. Surg. **108**: 163-177, 1938.
132. Murray, G., and Best, C. H.: Heparin and Thrombosis: The Present Situation, J. A. M. A. **110**: 118-119, 1938.
133. Murray, G., and MacKenzie, R.: The Effect of Heparin on Portal Thrombosis: Its Use in Mesenteric Thrombosis and Following Splenectomy, Canad. M. A. J. **41**: 38-40, 1939.
134. Murray, G., and MacKenzie, R.: Postoperative Thrombosis and Embolism, Am. J. Surg. **57**: 414-428, 1942.
135. Murray, D. W. G., Jaques, L. B., Perrett, T. S., and Best, C. H.: Heparin and Vascular Occlusion, Canad. M. A. J. **35**: 621-622, 1936.
136. Nelson, E. W., Jones, J. R., and Collins, C. G.: Pelvic Thrombophlebitis, A Study of the Etiologic Factors From a Statistical Standpoint, New Orleans M. & S. J. **95**: 375-381, 1943.
137. Neuhof, H., and Seley, G. P.: Acute Suppurative Phlebitis Complicated by Septicemia, SURGERY **21**: 831-842, 1947.
138. Neumann, R.: Centers of Origin and Formation of Development of Thrombosis of the Leg, Virchows Arch. f. path. Anat. **301**: 708-735, 1938.
139. Newburger, B.: Early Postoperative Walking; II. Collective Review, SURGERY **14**: 142-154, 1943.
140. Northway, R. O., and Buxton, R. W.: Ligation of the Inferior Vena Cava, SURGERY **18**: 85-94, 1945.
141. Northway, R. O., and Greenway, G. D.: Vena Cava and Its Collateral Circulation, Univ. Hosp. Bull., Ann. Arbor **10**: 67-69, 1944.
142. Ochsner, A.: Intravenous Clotting, SURGERY **17**: 240-259, 1945.
143. Ochsner, A.: The Use of Vasodilatation in the Treatment of Venous Thrombosis, Surg., Gynec. & Obst. **84**: 659-664, 15, 1947.
144. Ochsner, A., and DeBakey, M.: Rational Therapy on Vascular Thrombosis, New Orleans M. & S. J. **94**: 173-178, 1941.
145. Ochsner, A., and DeBakey, M.: The Role of Vasospasm in Thrombophlebitis and Its Treatment by Novocain Block of the Sympathetics, Tri-State M. J. **13**: 2654, 1941.
146. Ochsner, A., and DeBakey, M.: Therapeutic Consideration of Thrombophlebitis and Phlebothrombosis, New England J. Med. **225**: 207, 1941.
147. Ochsner, A., and DeBakey, M.: Therapy of Phlebothrombosis and Thrombophlebitis, Arch. Surg. **40**: 268, 1940.
148. Ochsner, A., and DeBakey, M.: Thrombophlebitis and Phlebothrombosis, South. Surgeon **8**: 269-290, 1939.
149. Ochsner, A., and DeBakey, M.: Thrombophlebitis, The Role of Vasospasm in the Production of the Clinical Manifestations, J. A. M. A. **114**: 117, 1940.
150. Ochsner, A., and DeBakey, M.: The Significance of Phlebothrombosis and Thrombophlebitis in Orthopedic Surgery, J. Bone & Joint Surg. **23**: 788-794, 1941.
151. Ochsner, A., and DeBakey, M.: Treatment of Thrombophlebitis by Novocaine Block of Sympathetics, SURGERY **5**: 491, 1939.
152. Ochsner, A., DeBakey, M., and Schroeder, G.: The Significance of Phlebography in Thrombophlebitis and Phlebothrombosis, J. A. M. A. **123**: 738, 1943.
153. Ochsner, A., and Dixon, J. L.: Superior Vena Cava Thrombosis, Review of the Literature and Report of Cases of Traumatic and Infectious Origin, J. Thoracic Surg. **5**: 641, 1936.
154. Olow, J.: Sur en detail concernant le diagnostic de la thrombose crurale, Acta obst. et gynec. Scandinav. **10**: 159-162, 1930.
155. Ophuls, W., and Dobson, L., cited by Rosenthal, S. R.: Thrombosis and Fatal Pulmonary Embolism, Arch. Path. **14**: 215, 1932.
156. Parsons, R. J., and McMaster, P. D.: The Effect of Pulse Upon the Formation and Flow of Lymph, J. Exper. Med. **68**: 353, 1938.
McMaster, P. D., and Parsons, R. J.: The Effect of the Pulse on the Spread of Substances Through Tissues, J. Exper. Med. **68**: 377, 1938.
157. Pendergrass, E. P., Chamberlain, G. W., Godfrey, E. W., and Burdick, E. D.: A Survey of Deaths and Unfavorable Sequelae Following the Administration of Contrast Media, Am. J. Roentgenol. **48**: 741, 1942.
158. Pfeiffer, D. B., and Sain, F. D.: Heparin and Dicumarol; Collective Review, Internat. Abstr. Surg. **78**: 109-119, 1944 (Surg., Gynec. & Obst.).
159. Pilcher, R. S.: Slowly Fatal Pulmonary Embolism, Lancet **2**: 942, 1938.
160. Pool, E. H.: Systematic Exercises in Postoperative Treatment, J. A. M. A. **60**: 1202-1204, 1913.
161. Portis, B., and Roth, H. A.: Prophylaxis and Treatment of Postoperative Thrombosis, S. Clin. North America **16**: 287-290, 1936.
162. Potts, W. J.: Pulmonary Embolism, Ann. Surg. **111**: 554-563, 1940.

163. Potts, W. J., and Smith, S.: Pulmonary Embolism: An Experimental Study of Variations in the Volume Blood Flow in the Inferior Vena Cava of the Dog, Arch. Surg. **42**: 661-664, 1941.
164. Priestly, I. T., and Barker, N. W.: Postoperative Thrombosis and Embolism: Their Treatment With Heparin, Surg., Gynec. & Obst. **75**: 193, 1942.
165. Putnoky, J., and Farkas, K.: Vergleichende pathologisch-histologische Untersuchung des Herzmuskels bei 1009 Obduktionen, unter besonderer Beachtung der Fälle von Thrombosen und Embolien. Virchows Arch. f. path. Anat. **287**: 400, 1932. Cited by Ochsner.[142]
166. Putzer, R.: Die Wadenvenen Thrombose in ihrer Beziehung Zur Architektur der Wade, Arch. f. Gynäk. **169**: 444-452, 1939.
167. Reich, C., Yahr, M. D., Eggers, C., and Lipkin, R.: Dicoumarol in the Prevention of Postoperative Thrombosis and Pulmonary Embolism, SURGERY **18**: 238-243, 1945.
168. Rhoads, J. E., Walker, J. J., and Panzer, L.: Control of Blood Coagulability With Coumarin and Other Drugs; Use of Basal Doses of Dicoumarol With Intramuscular Injections of Heparin for Sustained Anticoagulant Effect, Northwest Med. **42**: 182, 1943.
169. Richardson, M. H.: On Certain Unavoidable Calamities Following Surgical Operations, Boston M. & S. J. **151**: 583-588, 1904.
170. Ries, E.: Some Radical Changes in the After Treatment of Celiotomy Cases, J. A. M. A. **33**: 454-456, 1899.
171. Robertson, H.: A Clinical Study of Pulmonary Embolism, Am. J. Surg. **41**: 3-21, 1938.
172. Roessle, R.: On the Significance and Origin of Venous Thrombosis of the Lower Legs, Virchows Arch. f. path. Anat. **300**: 180-189, 1937.
173. Schnitzler, O.: Beitrag zur Verhutung der postoperativen Thrombose und Embolie durch Sympatol, Fortschr. d. Therap. **12**: 712-718, 1936.
174. Sgalitzer, M., and Kollert, V.: Kontrast austellung der Venen in Roentgen bilde, Klin. Wchnschr. **10**: 1659, 1931.
175. Shapiro, S., and Sherwin, B.: Studies in Thrombo-Embolization; II. Observations on the Use of Dicoumarol, Am. J. M. Sc. **205**: 206, 1943.
176. Shaw, W. F., and Richards, C. E.: Postoperative Exercises as Prevention of Embolism, J. Obst. & Gynaec. Brit. Emp. **45**: 451-455, 1938.
177. Shlevin, E. L., and Lederer, M.: Uncontrollable Hemorrhage After Dicoumarol Therapy With Autopsy Findings, Ann. Int. Med. **21**: 332-342, 1944.
178. Simpson, K.: Shelter Deaths From Pulmonary Embolism, Lancet **2**: 744, 1940.
179. Skillern, P. J., Jr.: On Aneurysmal Obstruction of Vena Cava Superior With Special Reference to the Caval Syndrome, International Clin. (27th S.) **1**: 75, 1917.
180. Smith, L. A., and Allen, E. V.: Vascular Clinics XIV Studies on the Rate of Venous Blood Flow; Physiologic Studies and Relation to Postoperative Venous Thrombosis and Pulmonary Embolism, Proc. Staff Meet., Mayo Clin. **16**: 53-57, 1941.
181. Snell, A. N.: Relation of Obesity to Fatal Postoperative Pulmonary Embolism, Arch. Surg. **15**: 237, 1927.
182. Sproul, E. E.: Carcinoma and Venous Thrombosis: The Frequency of Association of Carcinoma in the Body or Tail of the Pancreas With Multiple Venous Thrombosis, Am. J. Cancer **34**: 566-585, 1938.
183. Squier, R.: Management of Postpartum Phlebitis, S. Clin. North America **17**: 33-40, 1937.
184. Stich: Annual Session of the German Surgical Society, J. A. M. A. **105**: 525, 1935.
185. Stowers, J. M., and Grossman, M. E.: Thrombosis of the Inferior Vena Cava, Technique of Its Demonstration, Lancet, 868-870, 1946.
186. Storz, H.: Klinik der Thrombose und Embolie, Klin. Wchnschr. **17**: 257-260, 1938.[70]
187. Sylvan, F.: Vorbeugung und Heilung der Thrombose durch Heilgymnastik, Fortschr. d. Therap. **15**: 20-25, 1939.
188. Takaura, G.: Experimentelle Untersuchung über die Aetiologie der Thrombose, Arch. f. klin. Chir. **188**: 138-151, 1937.[146]
189. Thiebaut, B. R., and Ward, C. S.: Ligation of the Inferior Vena Cava in Thromboembolism, Surg., Gynec. & Obst. **84**: 385-401, 1947.
190. Veal, J. R.: Thrombosis of the Axillary and Subclavian Veins, Am. J. M. Sc. **200**: 27-29, 1940.
191. Veal, J. R.: The Prevention of Pulmonary Complications Following Thigh Amputations by High Ligation of the Femoral Vein, J. A. M. A. **121**: 240-244, 1943.
192. Veal, J. R., and Hussey, H. H.: Surgery of Deep Venous Thrombosis of the Lower Extremity, SURGERY **17**: 218-231, 1945.
193. Veal, J. R., Hussey, H. H., and Barnes, E.: Ligation of the Inferior Vena Cava in Thrombosis of the Deep Veins of the Lower Extremities, Surg., Gynec. & Obst. **84**: 605-610, 1947.
194. Veal, J. R., and McFetridge, E. M.: Primary Thrombosis of the Axillary Vein, Arch. Surg. **31**: 271-289, 1935.

195. Victor, J. A.: Clinical Considerations of Thrombosis and Embolism, Ann. Surg. **82**: 193-198, 1925.
196. Virchow, R.: Beitr. Z. Exper. Path. U. Phys. H. **2**: 1, 1846. Cited by McCartney.[116]
197. Von Jaschke, R. T.: Neuere Erfahrungen im Kampf gegen die postoperative Thromboembolie, Chirurg **9**: 274-278, 1937.[146]
198. Von Schrotter, in Nothnagel: Handbuch der Pathologie und Therapie, Vienna, 1901, Alfred Holder, 15/13:533. Cited by Kaplan.[88]
199. Wagner, K.: Symptomatology of Stenosis With Occlusion of Lumen of Superior Vena Cava, Polska gaz. lek. **11**: 61, 81, 1932.[153]
200. Walker, J., and Rhoads, J. E.: Effect of Dicoumarol on Susceptibility to Action of Heparin, SURGERY **15**: 859-865, 1944.
201. Wangensteen, O. H.: The Therapeutic Problem in Bowel Obstructions, Springfield, Ill., 1937, Charles C Thomas, p. 360.
202. Wasserman, L. R., and Stats, D.: Clinical Observations on the effect of 3.3'-methyl-Enebis (4-Hydroxycoumarin), Am. J. M. Sc. **206**: 466-474, 1943.
203. Waterfield, R. L.: Biot's Respiration in Superior Vena Cava Obstruction, Guy's Hosp. Rep. **78**: 305, 1928.
204. Welch, C. E., and Faxon, H. H.: Thrombophlebitis and Pulmonary Embolism, J. A. M. A. **117**: 1502-1508, 1941.
205. Westman, S. K.: Thrombophlebitis in Obstetrics and Gynecology, Lancet **2**: 421-424, 1936.
206. White, P. D.: Pulmonary Embolism and Heart Disease: Review of Twenty Years of Personal Experience, Am. J. M. Sc. **200**: 577-581, 1940.
207. Wilson, L. B.: Fatal Postoperative Embolism, Ann. Surg. **56**: 809-817, 1912.
208. Wright, H. P.: Changes in Adhesiveness of Blood Platelets Following Parturition and Surgical Operations, J. Path. & Bact. **54**: 461-468, 1942.
209. Wright, H. P.: Adhesiveness of Blood Platelets in Normal Subjects With Varying Concentrations of Anticoagulants, J. Path. & Bact. **53**: 255-262, 1943.
210. Yahr, M. D.: The Treatment of Thrombophlebitis, Surg., Gynec. & Obst. **80**: 615, 1945.
211. Zambellini, F.: A Case of Obliteration of the Cava Superior (Extract), Lodi Tipolitograf C. Dell'avo, 1900.[153]
212. Zava, L.: Sui vantaggi del levar precoce degli operati, Policlinico (sez. prat.) **47**: 865-872, 1940. Cited by Ochsner.[146]
213. Ziak, cited by Aschoff, L.: Ueber Thrombose und Embolie, Wien. klin. Wchnschr. **51**: 1277, 1938.
214. Zucker, H. D.: Clinical Experiences With Dicoumarol: Report of Eighteen Cases, J. A. M. A. **124**: 217-220, 1944.

Review of Recent Meetings

FIFTY-NINTH ANNUAL SESSION OF THE SOUTHERN SURGICAL ASSOCIATION

HOLLYWOOD BEACH, FLA.

J. HARVEY JOHNSTON, JR., M.D., JACKSON, MISS.

Aneurysm Following Surgical Procedures, D. C. Elkin, Emory University, Ga.—Surgical trauma with resultant arterial injury occasionally produces arteriovenous fistulas. Such postoperative shunts are not infrequently found in amputation stumps or following hysterectomy, thyroidectomy, or thoracentesis, yet may follow any operation. Mass ligation of tissue containing multiple vessels should be avoided because it may be productive of arteriovenous aneurysms. Elkin presented six personal cases of aneurysm following surgical procedures: (1) Aneurysm of right brachial artery following venepuncture; (2) arteriovenous fistula of uterine vessels one year following hysterectomy for fibroids; (3) arteriovenous shunt of facial vessels subsequent to local anesthesia for tooth extraction; (4) aneurysm of external iliac artery due to trauma of inguinal hernioplasty; (5) arteriovenous aneurysm of left radial vessels at antecubital space following incision and drainage of abscess; and (6) renal vessel arteriovenous communication subsequent to nephrectomy. **Barney Brooks** reported three aneurysms following surgical trauma: two of the femoral artery following hernioplasty, and one following amputation. **J. M. T. Finney, Jr.,** cited a personal case in which the patient died of shock and collapse on the twelfth postoperative day following cholecystectomy for acute cholecystitis. Autopsy disclosed massive retroperitoneal hemorrhage due to rupture of a traumatic aneurysm of the right renal artery. This was unquestionably due to the force of a Deaver retractor traumatizing the vessel against the body of a lumbar vertebra. Finney warned against the use of such sharp-edged retractors. **Deryl Hart** told of a patient who had profuse gastrointestinal hemorrhages following a cholecystectomy in which deep sutures were taken in the liver bed to control bleeding. Operation revealed profuse bleeding from a false aneurysm, which had ruptured into the common duct. Bleeding was so brisk from an opening in the liver that control was difficult; it was, however, accomplished by packing the opening with muscle and suturing. Unfortunately, the patient left the hospital against advice and died at home of massive intraperitoneal hemorrhage. **J. E. J. King** cited a most interesting case depicting the danger of ligation of vessels with large suture such as umbilical tape. This patient presented a large arteriosclerotic aneurysm of the abdominal aorta. Bilateral lumbar sympathectomy caused the aneurysm to decrease to approximately one-half its original size. The sac was subsequently encased with cuffs of fascia lata and the aorta ligated proximally with umbilical tape. Death ensued at a later date from massive gastrointestinal hemorrhage. Post-mortem examination showed that the umbilical tape had eroded into the duodenum with resultant bleeding.

Arterial Aneurysm of the Left Common Iliac Artery Secondary to Arteriovenous Fistula of Left Popliteal Vessels, J. M. Donald, Birmingham.—A case report of a 61-year-old Negro man who had been shot through the left knee forty-three years previously was given. Large varicosities of the left lower extremity had been present for thirty-eight years. Examination revealed a pulsating mass with a continuous thrill over the left popliteal space; the left iliac artery was fusiformly dilated and presented as a pulsating mass with a systolic bruit. Treatment consisted of ligation and excision of the popliteal arteriovenous shunt. Six months later there had been a regression of the iliac aneurysm to approximately one-third its original size. In reviewing the literature, Donald was able to find nine similar cases in

which an aneurysm of the proximal artery was associated with an arteriovenous fistula. In discussion, **Barney Brooks** pointed out the uncertainty of diagnosing a proximal aneurysm in such cases, as there is always tortuosity and dilatation of the artery in arteriovenous shunts.

Surgical Aspects in the Treatment of Aneurysms of the Aorta, Arthur H. Blakemore, New York.—An analysis of sixty-three cases of aneurysm of the aorta which had been treated surgically was given. There were twelve hospital deaths in this series, or a mortality of 19 per cent. Seventeen, or 27 per cent are now living; fifteen of these seventeen are carrying on normal activities. Treatment consisted of surgical exposure of the aneurysm with "controlled" stimulation of blood clotting by an electrothermic method, utilizing a 10 cm. segment of wire introduced into the aneurysm for ten seconds. Following production of the clot, impure polythene film was wrapped about the sac to produce chemical inflammation and fibrosis. A layer of pure, nonirritating polythene was used to overlay the first layer of polythene and limit the chemical inflammation. Blakemore found the electrothermic method of coagulation successful if the diameter of the orifice of the aneurysm was not greater than the diameter of the sac. The method has been sufficiently standardized so that there is little technical difficulty; most of the hospital deaths were due to the severity of the disease and not to the surgical treatment per se. This method should be more extensively studied as it holds promise of avoiding death from rupture of aneurysms and affords dramatic relief of pain with rehabilitation in some cases. **E. F. Parker** cited a personal case in which a ruptured aneurysm of the thoracic aorta was treated by proximal ligation. The patient survived two weeks without evidence of urinary suppression, but died of subsequent rupture with hemorrhage. **James Owings** has treated seven patients by the Blakemore method; there were excellent results in two. **A. O. Whipple** praised Blakemore for his untiring efforts in combating a heretofore hopelessly progressive disease.

Endometriosis, Joe V. Meigs, Boston.—The increased incidence of endometriosis seems directly related to late and infrequent childbearing. The disease is much less frequently seen in ward than in private cases. Meigs condemned the fact that our economic system is favoring late marriage and deferred pregnancy. Endometriosis is most commonly encountered in the age group from 30 to 50 years. The importance of acquired dysmenorrhea as a diagnostic point has been overemphasized, for in 32 per cent the pain was not dysmenorrheic. Infertility is important in the differential diagnosis of pelvic conditions, because it is so frequently associated with endometriosis. Meigs was emphatic in condemning oophorectomy as the treatment of choice. Although castration will cause regression and disappearance of endometrial implants, such patients are often more miserable as castrates than they were with the original disease. Oophorectomy should be reserved for those 45 years of age or older. Chocolate cysts of ovaries should be carefully shelled out. Bowel implants should be resected and not treated by castration. Testosterone has proved its value in selected cases.

In the discussion, all concerned heartily agreed in advocating conservatism in the treatment of endometriosis. Every attempt to salvage ovarian function must be made. **Curtis Tyrone** found endometriosis in 23 per cent of his private patients who had a pelvic laparotomy. **Walter Holmes** suggested observation when a diagnosis of endometriosis is made. Many of the associated symptoms will abate spontaneously. If surgery becomes necessary, hysterectomy with conservation of some ovarian tissue will frequently be the procedure of choice. Holmes agreed that bilateral oophorectomy was worse than the disease. **John Burch** stated that endometriosis is not such a progressive disease as is commonly believed. Observation has proved successful in most instances. The disease is characterized by a relatively low malignant potential. Burch contended that opening of endometrial cysts is all that is necessary in some cases. **Roger Doughty** rose to support further the conservative therapy in this disease.

Treatment of Acute Pancreatitis With Report of Cases, Mims Gage, New Orleans.—The etiologic factor in acute pancreatitis is reflux of bile into the pancreatic duct. This reflux is due to calculi in only 4 per cent of cases; spasm is much more likely to be the cause.

Rienhoff and Pickrell have shown a common ductal channel of the common and pancreatic ducts in 32 per cent of dissections. Gage showed a series of cholangiograms in which a reflux of lipiodal into the duct of Wirsung was evident. Severe acute pancreatitis may be associated with tetany; this is the result of hypocalcemia due to neutralization of the fatty acids in the areas of fat necrosis with calcium. The pain is of such severity that the diagnosis should be immediately considered. Confirmation with serum amylase studies is essential for diagnosis. Conservative treatment has proved to be the one of choice. In addition to the usual measures, such as transfusions, infusions, parenteral calcium, duodenal drainage, and sedation, Gage strongly advocated bilateral splanchnic block. This block not only dramatically relieves the excruciating pain, but seems to abort the pathologic process by overcoming the spasm of the blood vessels, common duct, and sphincter of Oddi. Six cases with no mortality in which the course of the disease was shortened and made less severe were cited. Approximately 65 per cent of the patients with acute pancreatitis have associated gall bladder disease and will require interval surgery.

Keith Grimson pointed out that splanchnic block interrupts visceral pathways to relieve pain, and warned against overlooking ruptured ulcer or acute cholecystitis. Certainty of diagnosis would be necessary before producing splanchnic anesthesia. **W. D. Gatch** stated that cessation of pain in acute pancreatitis is an ominous sign. **Alton Ochsner** stressed the importance of serum amylase determinations in the diagnosis. He is convinced that splanchnic block does much more than relieve pain; it halts the progress of the disease by overcoming the ductal and vascular spasm.

The Clinical Evaluation of Cholangiograms, Hart Hagan and **H. L. Townsend,** Louisville.—The need for more frequent cholangiography was stressed. Delayed cholangiograms should be routine procedure in all cases with T-tube or catheter drainage and fistulas. The value of immediate cholangiography has not been appreciated fully because its use has been restricted. That cholangiograms at the time of initial surgery are a valuable adjunct to the diagnosis of abnormalities of the biliary system, including stone, spasm, and strictures, is stressed. Employing immediate visualization will frequently broaden the scope of the primary operative procedure and thereby lessen the frequency of secondary operations. As there is no predicting when it will be needed most, it is urged that a casette and plate be properly placed as a routine procedure in biliary surgery. Excellent cholangiographic studies depicting the pathology frequently encountered were presented.

Acute Cholecystitis, J. W. Barksdale and J. Harvey Johnston, Jr., Jackson, Miss.—The importance of regarding acute obstructive cholecystitis as a surgical emergency was emphasized. Although a six- to eight-hour period of preoperative preparation is essential to restore electrolyte and fluid balance, surgery is then indicated. Most authorities agree that it is often impossible to determine the underlying pathology by laboratory-clinical methods; too often the disease advances to the stage of gangrene, empyema, and peritonitis with so-called conservative therapy. Barksdale and Johnston believe "watchful waiting" in reality to be "wishful waiting." It is somewhat of a paradox that a policy of diligent observation is universally accepted as being an unsound one in acute appendicitis, but is all too frequently employed in acute cholecystitis. Instituting operative therapy before the period of complication (gangrene, empyema, and perforation) would obviously decrease the mortality and morbidity of the disease. Cholecystectomy is feasible in above 90 per cent of cases and is the procedure of choice in trained hands. Cholecystostomy should be reserved for those in whom the general condition is precarious or the local pathology so marked that identification of vital structures is not feasible. By questionnaire, it was determined that 67 per cent of the members of the Southern Surgical Association favored early operation in acute cholecystitis, 25 per cent preferred delayed surgical intervention, and 8 per cent utilized careful individualization to decide therapy.

W. H. Parsons regretted that so many of the patients he treated were first seen with advanced cholecystitis—usually ninety-six or more hours after onset of the disease. Any form of therapy at this time has its drawbacks, making meticulous individualization of cases

essential. Stress was laid to the frequency of common duct stones in association with acute cholecystitis; **Parsons** has found a 50 per cent incidence of choledocholithiasis in his more recent acute cases. **J. Harvey Johnston** presented a series of 140 cases in which early operation (effected within the first seventy-two hours after the onset of symptoms) had proved to be much safer than conservative treatment. However, delayed intervention was the procedure of choice if at all possible in the period from four to eight days after the beginning of the illness.

Transverse Incisions in Lower Abdominal Surgery, John C. Burch, H. T. Lavely, Jr., and **Cloyce F. Bradley,** Nashville.—Transverse incisions of the Cherney type are especially useful in gynecologic and pelvic surgery. In the past few years, this approach has been used in over sixty cases with uniformly good results. Although the period of follow-up has been too brief, the authors have noted no wound weakness or hernias in their personal cases. Transverse incisions do require more operative time for execution; some difficulty in resuturing the rectus muscles to the pubis is not infrequently encountered. Burch believes these disadvantages are minor considerations when one considers the excellent exposure obtained for all pelvic surgery. He has found this incision to make Wertheim procedures technically much more feasible. **Joe V. Meigs** did not share this enthusiasm for transverse incisions. In a personal series of 150 cases he found the incidence of hernias to be too high. He favors a midline incision for radical pelvic surgery and questions better exposure with transverse incision.

Traumatic Wet Lung. An Experimental Study, Rollin A. Daniel, Jr., and **William R. Cate, Jr.,** Nashville.—The etiology of wet lung secondary to trauma and surgery was studied in dogs. A falling weight was used to produce controlled injury. This resulted in typical traumatic wet lung in the animals. As in human beings, fluid was found in parts of the lungs not subjected to trauma. The exact mechanism of this phenomenon is not known. These investigators found that simultaneous bleeding at the time of injury decreased the amount of fluid in the lungs. Animals, which had been subjected to previous cervical vagotomy, were given intravenous saline solution at the time of injury; nine of fifteen so studied developed a marked wet lung. However, if both a cervical sympathectomy and vagotomy had been done, controlled trauma and intravenous saline solution resulted in appreciable moisture in only one of seven. Daniel and Cate thus concluded that a reflex mechanism exists which plays a part in the pathogenesis of wet lung. In discussion, **J. M. Mason, III,** stressed the value of intercostal nerve block, bronchoscopy, and endotracheal catheter aspirations in the treatment of post-traumatic wet lung.

Paralysis of the Face Supported With Facial Grafts, Barrett Brown and **Frank McDowell,** St. Louis.—Demonstration by color movies showed the dramatic cosmetic results obtainable by support of paralyzed faces with fascial grafts. It was emphasized that this operative procedure was not to be considered as a competitor to the various nerve operations for the relief of facial paralysis. It is frequently a valuable adjunct to such procedures, but is especially indicated when they have failed or are not indicated. The technique of passing strips of fascia lata, obtained from the patient's thigh with a Masson fascia stripper, from the temporalis muscle and fascia to the upper and lower lips was well depicted in the movies. Only a small incision over the temporalis muscle is necessary to effect the procedure; the fascial strips are then passed subcutaneously to the upper and lower lips with long straight needles. The elevation of the face given by this fascial support overcomes much of the facial asymmetry and aids in closing the eyelids. A most important phase of the ultimate result is teaching the patient to use the facial muscles less. In discussion, **Louis T. Byars** stressed the importance of overcorrecting the deformity; he stated that he had never seen a patient in which the fascial strips had been too tight.

Preservation of Jaw Function Following Surgery, Trauma, and Infection, Louis T. Byars, St. Louis.—Many fundamentals of maxillofacial surgery aiding in attaining maximum jaw function were emphasized with case reports. More frequent use of subperiosteal resection with temporary wire splinting was urged for benign tumors. This uniformly gave

excellent cosmetic and functional results, but is not applicable to malignant tumors. The importance of fixation of mandibular fragments following loss of substance to avoid contracture was stressed. This may be often accomplished with interdental wiring, but occasionally must be effected with internal bar fixation. In the operative treatment of temporomandibular ankylosis, adequate resection of bone to create a permanent false joint is necessary. **T. G. Blocker** presented several personal cases in which striking results had been obtained following extensive loss of mandible and overlying soft tissues as a result of gunshot injuries.

Prolapse of the Gastric Mucosa Through the Pylorus, Ira A. Ferguson, Atlanta.—Although prolapse of the gastric mucosa into the duodenum was formerly considered unusual, it is now found with increasing frequency as it is being looked for. In a series of 297 gastrointestinal series at the Henry Grady Hospital in Atlanta, 23 cases of herniation of the gastric mucosa through the pylorus were found, an incidence of 7.7 per cent. Six personal case histories, five of them of men, were reported. The symptomatology is not unlike that of peptic ulcer or any condition which produces pylorospasm. Diagnosis depends on careful x-ray interpretation; usually a characteristic mushroom deformity in the duodenal bulb with a "central streak" can be demonstrated. Occasionally the symptoms are so marked and refractory to conservative measures that surgery becomes necessary. Probably any procedure which resects the redundant mucosa and/or allows free passage to and from the duodenum would be successful. One of Ferguson's patients was treated surgically with resection of the mucosa and a Finney pyloroplasty; freedom of symptoms was obtained. The importance of considering this not infrequent entity in differential diagnosis of abdominal symptomatology was emphasized. One of the patients reported upon had had an appendectomy and subsequent cholecystectomy without relief before the diagnosis was established.

Mesenteric Vascular Occlusion With Special Reference to Venous Mesenteric Thrombosis Due to Causes Other Than Local Trauma and Infection, J. D. Rives, L. H. Strug, and **Irving Essrig,** New Orleans.—A series of nineteen cases of mesenteric vascular occlusion was presented. In thirteen, thrombosis was the cause of vascular occlusion; in six, embolism. The disease is a rapidly progressive one and passes through three stages: (1) period of intestinal cramps with associated hyperperistalsis, (2) period of intestinal obstruction, and (3) gangrene. The onset may be gradual, but is quite often sudden and dramatic. The symptomatology features pain, moderate distention, and shock after the development of massive gangrene. Jaundice, which has not been previously reported, was noted in four cases of this series. Although the results are poor, surgery with resection of involved bowel represents the only chance for cure. Of the eight patients in this series submitted to surgery, only one survived; this patient had twelve feet of bowel resected. Better results would be obtained if the diagnosis were established earlier and immediate surgery undertaken. The presence of copious peritoneal fluid is characteristic of these cases. The involved bowel is usually found in the pelvis; distention proximal and distal to the area of strangulation is equal.

Lymphangioma of the Mesentery, G. V. Brindley and **G. V. Brindley, Jr.,** Temple, Texas.—Mesenteric lymphangiomas are often denoted as "chyle cysts." Although there is usually a palpable abdominal mass with associated discomfort, the exact diagnosis is often not made until exploratory celiotomy is done. Excision has proved to be the treatment of choice when feasible; marsupialization is sometimes the necessary procedure, however. A case report was presented of a 4-year-old white male with the history of having an enlarged abdomen since birth, hospitalized because of abdominal pain. Palpation disclosed an abdominal mass. Roentgenologic studies including intravenous pyelograms were not diagnostic. At operation, a cystic mass ten inches in diameter filled the abdomen. As the jejunum was intimately incorporated into the mass, bowel resection with side-to-side anastomosis was done. Postoperative convalescence was entirely smooth and the child was well when seen six months later. This multilocular lymphangioma constituted one-seventh of the boy's total weight. **C. W. Mayo** commented on marsupialization of such cysts; this may

be the only feasible surgical therapy. When done, it is imperative that all cystic compartments be ruptured. Infection should be anticipated and treated prophylactically with the various antibiotics. Sclerosing solutions are occasionally of value in aiding obliteration. The mistake of removing the drains too early is frequently made. In 175 cases of mesenteric cysts encountered at the Mayo Clinic only 7 were lymphangiomas. **D. B. Cobb** presented the case report of a 3-year-old child who, at operation for intestinal obstruction, was found to have a lymphangioma of the small bowel mesentery. It was possible to remove the cyst without resecting the bowel. At a subsequent operation, a second cystic mass was excised.

Enterogenous Cysts of the Duodenum With Report of a Case, Which Is Most Unusual, If Not Unique, W. L. Peple, Richmond, Va.—A most interesting cause of duodenal obstruction was found in the case of a 69-year-old white woman. In 1924, this patient was treated for gastric ulcer, but had freedom of symptoms until digestive disturbances reappeared in the spring of 1947. X-ray studies revealed an obstructing tumor of the duodenum. At operation, an enterogenous cyst was found. This was successfully resected through an incision in the pylorus of the stomach. Review of the literature revealed this to be the fifteenth reported case of enterogenous cyst of the duodenum. This case is most unusual from the age standpoint; most of the reported cases were in infants less than 4 months of age. **Deryl Hart** presented another case of enterogenous cyst of the duodenum. His 15-year-old patient presented a palpable mass in the right upper quadrant of the abdomen. At operation, a larger, noncompressible mass which seemed to be continuous with the stomach was found. As resection was not feasible, this cyst was anastomosed to the duodenum. Although the patient has been completely free of symptoms since operation, Hart believes a Roux or Y type of jejunal anastomosis would be a better operative procedure.

Diverticulitis of the Jejunum Complicated by Jejunocolic and Jejunojejunal Fistulas: Case Report, Carrington Williams and **L. H. Bosher, Jr.,** Richmond, Va.—In a study of 350 cases of jejunal diverticulosis, 60 patients developed surgical complications. A most unusual complication was manifest in the case reported of a colored woman hospitalized because of marked weight loss and the passage of undigested food by rectum. Barium enema disclosed a free communication between the transverse colon and jejunum; this opening was not demonstrable by gastrointestinal series. At operation, numerous mesenteric and antemesenteric jejunal fistulas were found. In addition to the jejunocolic fistula shown by barium enema, eight jejunojejunal fistulas were evident. These fistulas were disconnected and the openings in the bowel closed. Six months later the patient was much improved but barium enema disclosed another fistulous communication between the jejunum and the splenic flexure. **L. H. Landry** told of a personal case involving a large tympanitic mass in the epigastrium. Roentgenologic studies disclosed a huge jejunal diverticulum with a definite fluid level. **L. W. Grove** commented on a patient seen recently who had intestinal obstruction as a result of several large diverticuli of the ileum. **J. E. J. King** operated successfully upon a patient with a similar condition in which the intestinal obstruction was due to two large jejunal diverticula.

Rationale and Results of Retropubic Prostatectomy, Ousley Grant and **Robert Lich, Jr.,** Louisville.—Prostatectomy is usually effected by one of three standard methods: (1) suprapubic, which has the disadvantage of passing through the bladder to reach a gland lying outside of the bladder; (2) perineal, which is a true surgical procedure and has the great advantage of removing the prostate gland and its capsule (it has the decided disadvantages of creating temporary urinary fistulas and not infrequent loss of sex potency); (3) transurethral, which does not permit radical removal of carcinoma. Millan of London has recently revived interest in retropubic prostatectomy. Grant believes that the fears heretofore held about the space of Retzius are unjustified. By this approach, all the advantages of perineal prostatectomy are obtained without the complications of incontinence and impotence. A series of fifty retropubic prostatectomies without mortality, without fistulas, and with no impotence was presented. Grant believes this method is so far superior to the standard procedures that comparison is incredible. In the discussion **H. W. McKay** said

he finds incontinence of one week to three months a usual sequela of perineal prostatectomy. **Guy Blackburn**, of London, has observed Millan perform this operation with great dispatch on any number of occasions. If retropubic prostatectomy follows a suprapubic cystostomy, a transverse incision has proved the one of choice in his hands. **Edgar Burns** expects to add the retropubic procedure to his therapeutic armamentarium, but believes each procedure has its individual merits. Grant concluded by stating that he and Lich have given up perineal prostatectomy. Hemorrhage has been minimal in the retropubic procedure; the operation can usually be completed in forty minutes.

Unusual Intracranial Lesions Producing Large Cranial Defects, J. E. J. King, New York.—A series of unusual intracranial lesions was depicted by x-ray pictures and lantern slides. Several large epidermoid cysts had been encountered. Diagnosis was established by the characteristic scalloped border with definite white line as found on roentgenologic examination. The defects resulting from excision of these large lesions were often closed, if the dura was intact, by cleaning and boiling the removed bone and replacing it as a bone graft. No untoward results were obtained from this practice. Another interesting case with a large extradural air pocket was reported. This was found to be due to a defect in the petrous portion of the temporal bone, which allowed the entrance of air.

Anatomical Observations on the Lumbar Sympathectics With Evaluation of Sympathectomies in Organic Peripheral Vascular Disease, G. H. Yeager and **R. A. Cowley,** Baltimore.—In a series of 162 patients with peripheral vascular disease who were subjected to sympathectomy, only 30 per cent were definitely improved. Feeling that nonfamiliarity with sympathetic anatomy may be partially responsible for the failures, careful anatomic studies were done on eighteen cases. Marked extremes of variation were found: no two cases were identically similar. No sex difference was noted. The most constant ganglion was that in relation to the second lumbar vertebra; it was usually found at the lower third, often extending on the intervertebral space. These anatomic studies showed only one of eighteen to have the four ganglia on one side, as is usually depicted in anatomy textbooks. **George Lilly** finds "sympathetic failures" are not infrequently due to not removing the sympathetic ganglia. In reoperating upon patients to effect an adequate lumbar sympathectomy, he finds it much easier to identify the chain if a posterior approach similar to the lower part of a Smithwick procedure is used instead of the usual anterolateral approach.

The Effects of Priscol (2-Benzyl-4, 5-Imidazoline HCl) on Vascular Diseases and Hypertension in Patients, Keith S. Grimson, F. A. Marzoni, M. J. Reardon, and **J. P. Hendrix,** Durham.—Priscol is more specific in its action than is tetraethylammonium chloride; it is able to block the action of adrenalin. Side reactions are not uncommon and include flushing, palpitation, nausea, "goose flesh," and occasionally postural hypotension. These are rarely serious or distressing. When administered to seventeen hypertensive patients in dosage of 100 to 200 mg., eight showed a temporary drop of blood pressure to normal, four others had some reduction, and five presented no change. The cold pressor test was decreased or abolished in ten of the seventeen patients. Priscol proved to be of no value in determining which hypertensive cases would have significant lowering of blood pressure following sympathectomy. In peripheral vascular disease, it is felt that Priscol is able to equal the effects of sympathetic blocks and is thus of value in determining suitable candidates for surgery. Four of six patients with causalgia were aided by taking the drug. The most striking therapeutic response was in Raynaud's disease. Even those patients who had previously had a sympathectomy seemed to be aided. The drug increases the tolerance to ice water in vasospastic functional disease. Priscol, in dosage of 25 to 75 mg., is apparently a valuable adjunct to the treatment of peripheral vascular disease.

The Differentiation of Hyperthyroidism, George M. Curtis, Columbus, Ohio.—Since basal metabolism determinations are not wholly specific in determining thyroid activity, studies have been conducted to determine other tests to ascertain the degree of thyroid function.

After many thousands of determinations, it is evident that the protein-bound blood iodine is directly correlated with thyroid function. As is well known, there is a tendency in some cases of nontoxic goiter to develop toxicity. If these patients have suggestive symptoms, the protein-bound blood iodine is greater than 1.2 μg per cent, and the basal metabolic rate above plus 4, Curtis believes incipient hyperthyroidism to be developing and advises operation. It is possible to differentiate hyperthyroidism from hypermetabolism by determining the protein-bound blood iodine. Thus menopause, anxiety states, multiple myeloma, etc., can be excluded. Curtis concluded by stating the determination of the protein-bound blood iodine to be of distinct value in the diagnosis of hyperthyroidism—more so than basal metabolic rate alone. However, the best way to ascertain thyroid activity is to determine the level of the protein-bound iodine in the blood and the basal metabolic rate. **Frank Lahey** stated that the Lahey Clinic results fully confirmed the value of protein-bound iodine determinations in the diagnosis of thyroid disease. The main disadvantage is that the determination is a difficult and painstaking one. A direct relationship of storm to protein-bound blood iodine exists. The test is of especial value in the diagnosis of the occasional case of hyperthyroidism associated with a normal basal metabolic rate. The status of propylthiouracil has now been clarified; it provides an excellent method of preparing patients, but is not a substitute for surgery. No matter how long the drug is given, the percentage of recurrence of hyperthyroidism is the same. The incidence of complications is 1.25 per cent as contrasted to 9 per cent for thiouracil. It is certainly not a drug to be used indiscriminately, for deaths from agranulocytosis do occur. It has eliminated trial subtotal thyroidectomy, however, for propylthiouracil will demonstrate what can be accomplished by surgery. Dosage varies from 200 to 400 mg. daily. Children and pregnant women should be given full adult doses. Psychotic and cardiac patients should be allowed to get completely well for two to three months before operation is undertaken. Radioactive iodine should be reserved for experimental studies for the time being; otherwise, its use will be abused. It produces a marked degree of thyroiditis. Because of the danger of malignancy, it should not be given to patients with adenomatous goiter. **T. C. Davison** emphasized the occurrence of hyperthyroidism without an increased basal metabolic rate. In those patients with tachycardia, palpitation, and weight loss, the results of the "tin-box" should be disregarded and the patient given a thorough trial with propylthiouracil. Davison considers thiouracil so dangerous that it should be outlawed as a drug. **Rawley Penick, Jr.,** stated that basal metabolic rates of -17 and lower were so frequent in the Gulf Plain section that they are considered normal. Hence, a reading of plus 10 per cent would represent a real increase in these individuals.

Hyperthyroidism in Absence of Discernible Goiter, Harold L. Foss, Danville, Pa.—The frequency of thyrotoxicosis without enlargement of the thyroid gland is emphasized. Although these patients have classical hyperthyroidism, their physicians are often misled by the normal size of the thyroid gland. Foss found 8.4 per cent of all patients admitted for thyroid overactivity to have less than 30 Gm. of tissue removed at operation. While the milder cases may be cured with propylthiouracil, surgical resection is necessary in the majority. This entity is most frequently encountered in males. **Frank Lahey** stated that the size of the thyroid is in no way related to toxicity. In men, the thyroid gland is deeper and lower than in women; thus, an actual enlargement may be difficult to demonstrate clinically. **Donald Guthrie** is in favor of abandoning the term "exophthalmic goiter."

Further Study of Carcinoma of the Breast in the Negro, Isidore Cohn, Alfred Longacre, and **Robert Waters,** New Orleans.—The incidence of carcinoma of the breast in the colored race has remained the same. The disease seems to appear at an earlier age in the Negro. The average duration of symptoms at the time of first examination has diminished but is still one to two years. Obviously, further education is essential to have the patients present themselves for treatment earlier. When admitted to the hospital, 62 per cent of the colored and 42 per cent of the white patients had clinical evidence of axillary metastasis. A notable increase in the use of breast biopsy has occurred in the past decade.

Cancer of the Breast, W. P. Nicholson, Jr., and **Edgar D. Grady,** Atlanta.—A series of 905 charity patients with carcinoma of the breast was presented; 417 of the group were

treated surgically. Since the series ended before 1942, no hormones were used. Two of the patients were under 25 years of age. Surprisingly, the rate of five-year survivals was as good in the 20 to 30 age group as in the 30 to 60. Pain alone was the presenting symptom in 5.3 per cent. Over 25 per cent of the malignancies had existed over one year. Less than 15 per cent had come in within one month of onset of symptomatology. The five-year survival rate was 18 per cent with positive axillary metastases; 54 per cent when the axillary lymph nodes were negative. Roentgen castration of patients in the premenopausal age group seems indicated. Although the series is small, a striking difference is noted: ten of eleven so treated survived five years. Simple mammectomy was done in patients over 60 years and in the poor operative risks. Following radical mastectomy, no swelling of the arm occurred in 56 per cent; 23 per cent had slight, 14 per cent moderate, and 7 per cent severe swelling. Eighty-six per cent of the malignancies were located at the upper half of the breast. Local recurrence occurred in 16 per cent. In discussion, **T. C. Davison** emphasized the striking difference in five-year survival rates in private and clinic patients: 55 per cent in the former and 28 per cent in the latter group. Testosterone in daily dosage of 50 mg. is helpful in those patients with osseous metastases.

Bacteriostatic Agents as Adjuvants to Anal Surgery, Curtice Rosser, Dallas.—Bacteriostatic agents are valuable adjuncts to the success of anal surgery: hemorrhoidectomy, fistulectomy, and sphincteroplasty. Reliance on constipating diets gives a false sense of security. Gelfoam or oxidized cellulose, when used as a covering to rectal wounds, seems to aid healing. Sulfone (NU-404) can be given without toxic effects and decreases the coliform bacterial count of the stool. It results in no change in the healing time of rectal wounds, but probably aids in increased function following fistulectomy. **A. R. Koontz** reminded the group that fibrin is converted into fibroblasts in the healing of wounds. Thus, frequent change of gauze dressings removes valuable fibrin and delays wound healing.

Current Trends in Surgery of the Distal Colon and Rectum for Cancer, A. S. Graham, Richmond, Va.—Fifty leading colon surgeons were contacted to determine their policies in the management of malignancies of the sigmoid, rectosigmoid, and rectum. A similar study in 1938 disclosed that most surgeons favored colostomy and stage resection of lesions of rectum and rectosigmoid. There is now a pronounced trend away from extraperitoneal procedures; primary anastomosis is increasingly favored. Routine proximal drainage is unpleasant and frequently unnecessary. Of the group consulted, 84 per cent use chemotherapeutic agents routinely; 36 per cent use one of these drugs locally at operation. The trend toward anterior resection for lesions of the upper rectum and rectosigmoid is apt to be short lived: 24 per cent never use the procedure, 58 per cent rarely, and only 18 per cent routinely. The classic abdominoperineal resection for rectal and rectosigmoidal lesions is used by 82 per cent; most prefer a one-stage procedure. In the discussion, **R. S. Daniel** of Los Angeles pointed out that the incidence of local recurrence following anterior resection was 15 per cent as compared to 3.4 per cent following abdominoperineal resection.

Familial Polyposis and Carcinoma of the Colon, W. L. Estes, Jr., Bethlehem, Pa.—Case reports of a remarkable family showing the marked familial tendency of diffuse polyposis of the colon with the strong probability of development of carcinoma were given. The mother died at the age of 41 years of cancer of the sigmoid. A 38-year-old daughter presents diffuse polyposis of the transverse and descending colon. A 29-year-old son presents similar lesions in the rectum and sigmoid. Both have refused surgery thus far. Another son, 25 years of age, has had an abdominoperineal resection for carcinoma of the rectum. He is alive and well five years postoperatively, but declines surgery for the numerous remaining colon polypi. A daughter died at the age of 24 years of carcinoma of the sigmoid superimposed on familial polyposis. Another member of the family died at the age of 29 years of cancer of the sigmoid; rectal polyposis had been detected eight years earlier. A 21-year-old daughter is alive with an ileosigmoidostomy following a colon resection for polyposis. There is no familial history of malignancy on the paternal side. Estes urged surgery in all cases of familial polyposis of the colon; he believes this to be a 100 per cent premalignant condition.

Complete colon resection with permanent ileostomy is usually the procedure of choice. Occasionally it will be possible to avoid an enterostomy by salvaging the rectum. **R. B. Cattell** reported a similar family group in which four children had multiple polyposis. The entity passes from generation to generation as a mendelian dominant. Total colectomy with ileostomy should be used in all cases because recurrence in the rectum is so likely. **C. W. Mayo** pointed out that 5 per cent of patients with colon polypi had polypi elsewhere, such as stomach, small intestine, etc.

Low Anterior Resection, With and Without Transverse Colostomy, C. W. Mayo, Rochester, Minn.—A comprehensive study of 200 unselected patients who had had low anterior resection for malignancy was carried out. All growths were from 5 to 15 cm. above the dentate margin. In 100 of the patients, complementary colostomy was done; in the other 100 no proximal decompressive or defunctionating procedure was carried out. The hospital mortality for the entire series of 200 was nine deaths, or 4.5 per cent. Only 3 per cent of those with colostomy died, while 6 per cent of those without colostomy died. However, four of the deaths in the latter groups were due to pulmonary embolism; thus, the corrected mortalities are not significantly different. The morbidity, as would be expected, was much higher in the colostomy group. While 82 per cent of those without colostomy were out of the hospital in one month, only 4 per cent of those with proximal enterostomy were. Mayo believes that low anterior resection has a definite place in the treatment of malignancies of the rectosigmoid and upper rectum, since retrograde lymphatic metastases are infrequent. He warns that careful case selection is essential, and urges that one get at least 2 cm. below the lesion to minimize recurrence. In discussion, **R. S. Daniel** reported forty-four personal cases of primary aseptic anastomosis following colon resection for malignancy. There were no deaths in the series. On the other hand, there were two deaths in a group of seven colon resections of the Mikulicz type. **R. G. Doughty** stressed the not infrequent occurrence of multiple primary malignancies in the colon. He cited a personal history in which the patient had multiple carcinoma of the sigmoid. **R. B. Cattell** and the surgical staff of the Lahey Clinic favor one-stage abdominoperineal resection for malignancies of the rectum and rectosigmoid. In a series of 383 abdominoperineal resections done from 1942 to 1945, only two two-stage procedures were done. Cattell questions one's ability to determine clinically ideal cases for anterior resection; he believes abdominoperineal resection should be employed routinely. Sulfathaladine is used preoperatively. Intraperitoneal antibiotics, that is, 200,000 units of penicillin, are used only when contamination occurs. Sulfa drugs are not used locally.

The Present Status of the Problem of Gastric Cancer, R. Lee Clark, Jr., Houston.—Review of the literature reveals an increasing resectability with a decreasing mortality for gastric cancer. In 1805, resection was done in only one in 200 patients; now one in three have gastric resection. The mortality has steadily declined from 75 to 5 per cent. Every effort to establish earlier diagnosis must be instituted, for here lies the great fallacy in present-day treatment. In spite of increasing resectability and lowering operative mortality, a patient with a gastric carcinoma has only a 5 per cent chance of five-year survival. Of the few fortunate enough to have gastric resection before lymph gland metastasis has occurred, 50 per cent survive five years. Every gastric ulcer should be regarded as a malignant one and treated surgically. In discussion, **Alton Ochsner** emphasized that treatment must be instituted before the diagnosis can be made by present-day standards. Every lesion must be treated as a carcinoma. Although roentgenograms are considered 90 per cent accurate in our present concept of gastric cancer, exploratory operation should be advised in those with weight loss and stomach complaints, even though roentgenologic studies are negative. **Frank Lahey** urges more total gastrectomies in the therapy of gastric malignancy. Since follow-up is so difficult, surgery should be advised for all gastric ulcers; one in ten are malignant. **Joe Meigs** cited two recent cases in which carcinoma in situ of the stomach was diagnosed by cytologic studies of the gastric juice. It is likely that extension of such studies will result in earlier diagnosis. **G. Blackburn** reported lowering of operating time in total gastrectomy by using two teams, one thoracic and the other abdominal.

The Surgical Treatment of Peptic Ulcer; A Comparison of the Results of Gastroenterostomy, Gastric Resection and Vagotomy at the Duke Hospital, C. E. Gardner, Jr., and **Deryl Hart,** Durham. An analysis of 265 surgically treated patients with peptic ulcer is given. Gastroenterostomy was done in 68 cases; it is the procedure of choice in older patients with cicatricial ulcer and pyloric obstruction. Hospital mortality was 7.3 per cent for the group; 88 per cent were relieved of symptoms. Malfunctioning stomas were present in 19 per cent; in 3 cases, secondary operation was necessary. Subtotal gastric resection was employed in 123 cases. Over-all hospital mortality was 8.9 per cent. If the patients with massive bleeding are excluded, the rate is lowered to 6.6 per cent. Five of the 8 deaths were due to injuries to structures about the duodenal stump: 2 duodenal leaks, 2 injuries to the common duct, and 1 damaged hepatic artery. Postoperative gastric retention occurred in 14 per cent of the patients; 84 per cent were relieved of symptoms; 5 per cent presented recurrences. Pyloric exclusion procedure was used in 27 per cent. Vagotomy was done in 77 patients and 80 per cent were improved; 36 per cent presented postoperative gastric retention; one-third of these (14 per cent of the total) required a secondary operation. Eight per cent complained of persistent intestinal cramps and diarrhea following vagotomy. The only death in the group resulted from rupture of a hugely distended stomach. As a result of their critical analysis, Gardner and Hart concluded: (1) none of the operations employed for the therapy of peptic ulcer give uniformly satisfactory results; (2) gastroenterostomy is applicable in only a few cases, but is the procedure of choice in elderly patients with cicatricial stenosis; (3) gastric resection remains the procedure of choice at this time; (4) vagotomy is contraindicated in the presence of hemorrhage, gastric ulcer, and pyloric obstruction. The status of vagotomy in association with gastroenterostomy or pyloroplasty is being determined. The greatest indication at present for vagotomy is marginal ulcer.

In discussion, **L. W. Grove** presented a personal series of 150 gastric resections with only one death, a mortality of 0.66 per cent. Three-fourths were of the Hofmeister antecolic type. **F. W. Bancroft** remarked that vagotomy is usually a first step operation for peptic ulcer. **Hart** emphasized that vagotomy can paralyze the stomach and thus it disturbs the stomach as much as resection. He believes vagotomy should be restricted to experimental projects until its indications and dangers are determined.

Surgical Treatment of Obstructive Lesions of the Esophagus, James M. Mason, III, Birmingham.—Brief case reports with illustrative roentgen studies of the usual obstructive lesions of the esophagus were given. Transabdominal esophagogastrostomy of the Finney type was favored for esophageal achalasia. The feasibility of resecting high esophageal lesions and effecting satisfactory intrathoracic esophagastrostomy was emphasized. An excellent result was obtained in a complete lye stricture of the cervical esophagus; a plastic procedure through an approach anterior to the sternomastoid was used to re-establish continuity.

Alton Ochsner opened the discussion by stressing the two bugbears of esophageal surgery which persist despite antibiotics: (1) contracted blood volumes, so frequently encountered in malignant disease and chronic infections, must be corrected if the patient is to withstand such massive surgical procedures; (2) anastomotic strictures remain a source of postoperative concern; these may be avoided if particular attention is paid to maximum enlargement of the severed end of the esophagus. The case report of a successfully resected carcinoma of the upper thoracic esophagus in a 77-year-old colored man was presented. **Dailey** emphasized three essentials of postoperative management: (1) avoidance of administering intravenous saline solution, thereby lessening anastomotic edema; (2) not passing the Levine tube through the site of anastomosis; and (3) allowing liquids as soon as the patient reacts, for they will cause no more harm than swallowed saliva. **Edgar Davis** prefers transthoracic esophagogastrostomy for achalasia.

Preliminary Report on the Use of Tantalum Mesh in the Repair of Ventral Hernias, Amos R. Koontz, Baltimore.—Realizing the need for improvement in the results of large ventral hernias, Koontz used tantalum mesh in experimental animals to determine its clinical value. In four dogs, the rectus muscles were resected. Repair was effected by interposing

tantalum mesh between the peritoneum and subcutaneous tissue. In all four animals, a secure repair with no gross or microscopic tissue reaction was obtained. The experimental results were so gratifying that he used the method in five clinical cases—all patients with large or recurrent hernias. To date, each of the five repairs has been completely successful. In each case, the usual repair was re-enforced with a layer of tantalum mesh. Follow-up roentgenograms showed some fragmentation of the mesh, but no symptoms whatsoever were associated. All dead space should be carefully obliterated; it is essential to cover the mesh with skin that has attached subcutaneous tissue. Subsequent laparotomy is feasible, for the mesh can be cut with ordinary surgical scissors. **J. M. T. Finney, Jr.**, praised Koontz for his continued endeavors in overcoming the problem of large and recurrent hernias. **W. J. Prioleau** finds alloy steel wire to be the suture of choice in hernioplasty.

Spontaneous Perineal or Para-Rectal Hernia, Thomas Harrold, Macon, Ga.—The case report of a spontaneous levator or perineal hernia in a 36-year-old white man was presented. There had been no antecedent trauma. The patient complained of intermittent painful swelling to the left of the rectum. Examination revealed a 5 by 8 cm. mass in the left ischiorectal fossa. At operation, a fibromatous mass and hernial sac were excised; the opening in the levator muscle was closed with interrupted sutures. Pathologic study of the excised mass revealed it to be a fibrous hemangioma. In a review of the literature, five of the eight cases were associated with tumors, one of which was malignant. Thus, tumors seem to play a prominent part in the etiology of pararectal hernias.

Comparison of War and Civilian Experiences in Management of Perforating Abdominal Wounds, David H. Poer, Atlanta.—The recent war standardized the treatment of perforating abdominal injuries and lowered the mortality from 50 to 19 per cent. This was effected by better appreciation of the underlying pathology and the pathogenesis of shock, an increased knowledge of protein and electrolyte balance, and the routine use of chemotherapeutic and antibiotic agents. The importance of complete diversion of the fecal stream in wounds of the colon and rectum was emphasized. While the time factor is most important prognostically, multiplicity of wounds to intra-abdominal viscera is even more important. Oglivie has aptly classified deaths within the first two hours as due to hemorrhage, within the first two days as due to shock, and within the first two weeks as due to infection. **Pat R. Imes** emphasized the use of multiple transfusions in lowering mortality. He is not in full accord with the concept of fecal diversion in colon injuries. In a series of 168 such injuries in the Mediterranean theater treated by primary suture, there was a mortality of 12 per cent, which compares favorably with results obtained by exteriorization. **Ambrose H. Storck** urged the development of protective armor against atomic energy. **G. Blackburn** agreed with Imes in primary suture of colon injuries.

Construction of a Vagina With the Use of Skin Grafts and Vitallium Mold, Walter R. Holmes, Atlanta.—Excellent anatomic and functional results were obtained in three patients with congenital absence of the vagina. By careful sharp and blunt dissection a space between the vagina and rectum was developed. A split-thickness graft everted over a suitable vitallium mold was then inserted; care was taken to suture the edge of the graft to the vestibular mucosa. Approximation of the labia mucosa aids in immobilization of the mold and graft. Attention was called to the frequent association of urinary tract anomalies with congenital absence of the vagina. Each of these three cases had such congenital anomalies.

T. G. Blocker, Jr., presented a personal series of six patients treated by this method. He utilized an acrylic mold with an enlarged cephalic end; this remained in place well. **L. R. Wharton** stated that this method of construction of an artificial vagina was so simplified that it was the procedure of choice. Dissection of a wide space is essential to gain adequate depth; skin grafts should be used in every case. Making the mold of proper form is of more importance than is the material from which the mold is made. Postoperative care should feature daily dilatation; large Pyrex test tubes function as excellent dilators.

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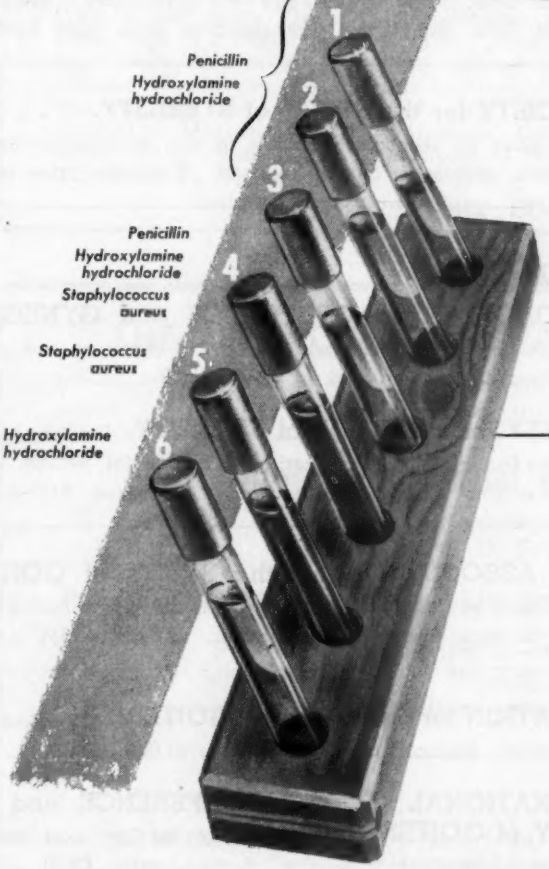

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